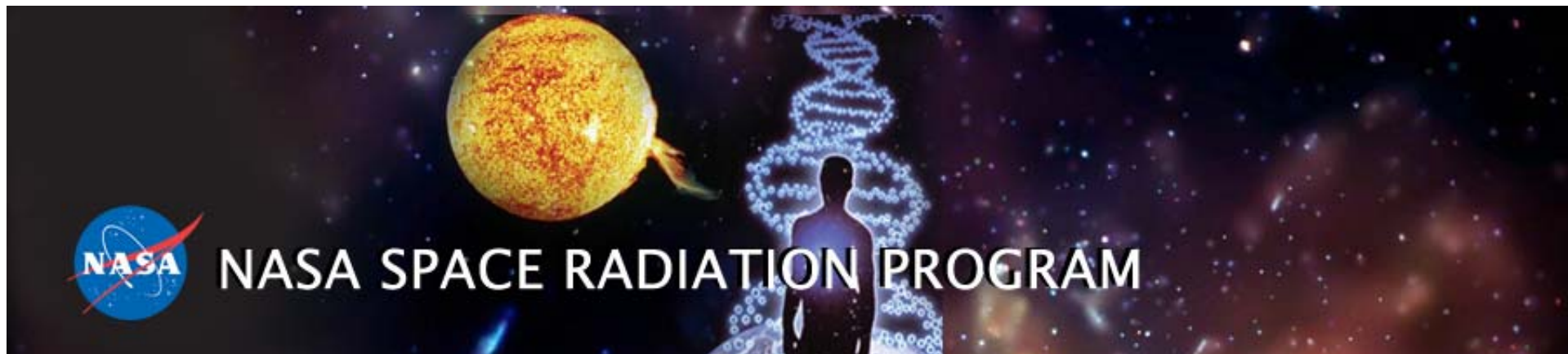




Stochastic models of DNA damage by high-energy particles

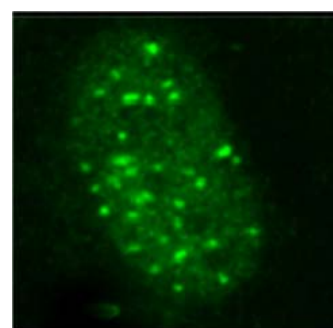
**Ianik Plante
Universities Space Research Association
Division of Space Life Sciences
NASA Johnson Space Center, Houston TX**

59th Annual Meeting of the Radiation Research Society
Hilton New Orleans Riverside, New Orleans, LA 70140
September 14-18, 2013

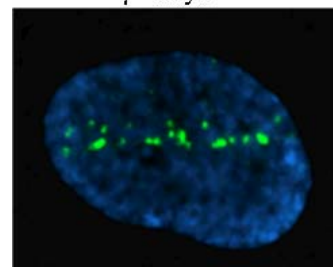


The space radiation problem

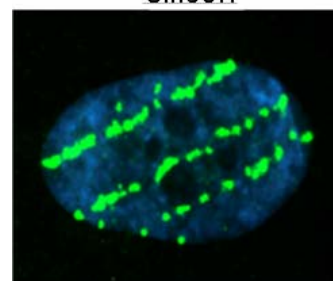
- ❑ Space radiation is comprised of high-energy protons and heavy ions (HZE's) and secondary protons, neutrons, and heavy ions produced in shielding
- ❑ Unique damage to bio-molecules, cells, and tissues occurs from HZE ions that is qualitatively distinct from X-rays and gamma-rays on Earth
- ❑ No human data to estimate risk from heavy ions, thus requiring use of biological models and theoretical understanding to assess and mitigate risks
- ❑ Shielding has excessive costs and will not eliminate galactic cosmic rays (GCR)



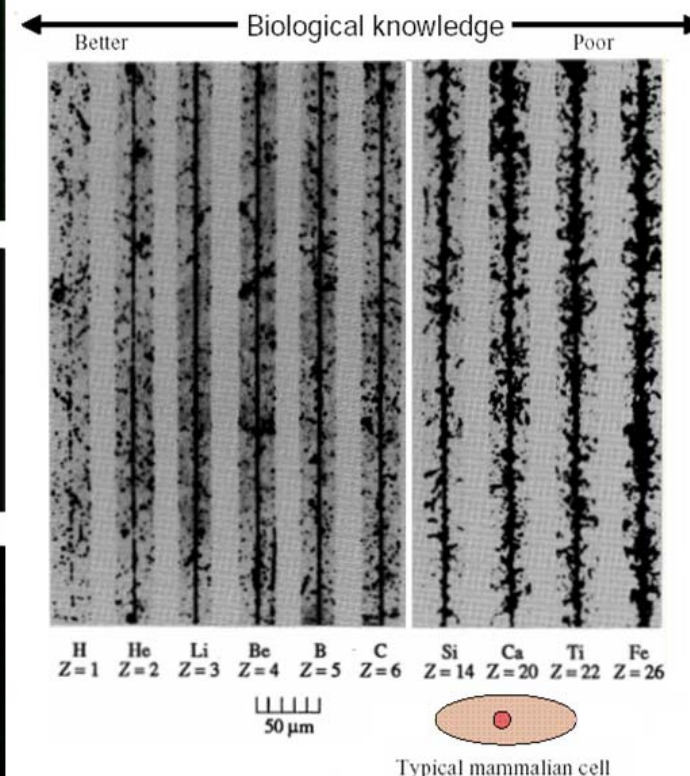
γ - rays

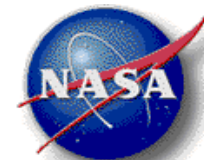


silicon



iron

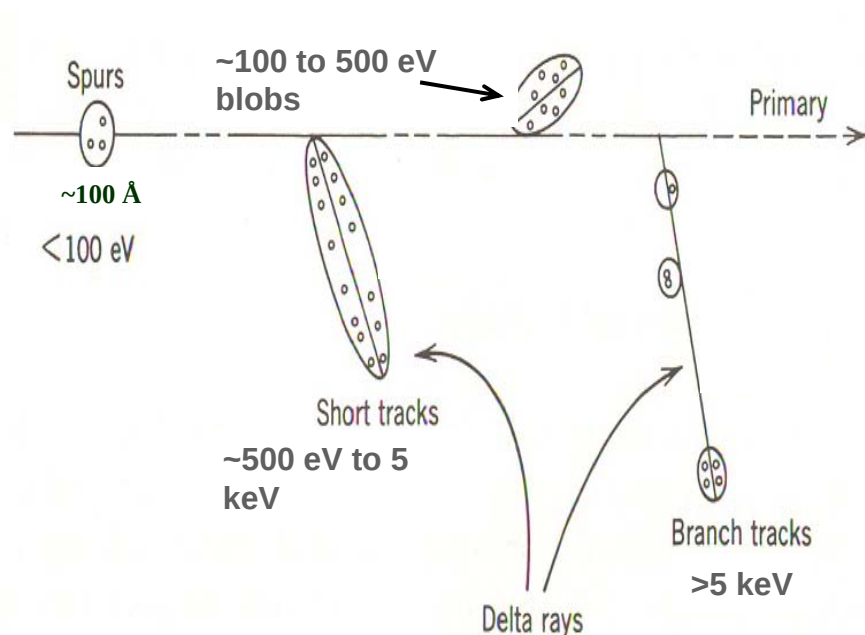




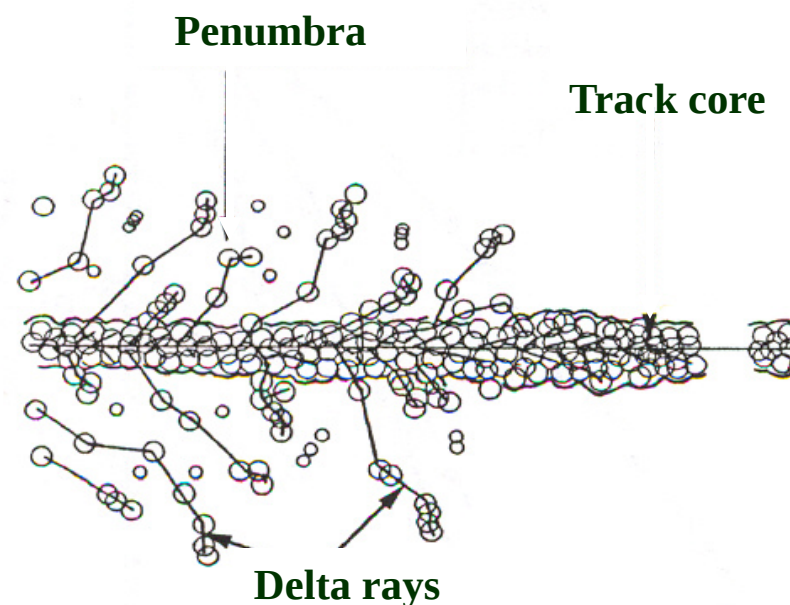
Radiation tracks and energy deposition

- ❑ The energy deposition by heavy ions is highly heterogeneous and dependent on the type and energy of the ion
- ❑ The interactions of radiation with matter are stochastic in nature and therefore often studied by Monte-Carlo simulations

Primary energy loss events in low-LET tracks



Primary energy loss events in high-LET tracks



A. Mozumder and J.L. Magee (1966) *Radiat. Res.* **28**, 203

C. Ferradini (1979) *J. Chim. Phys.* **76**, 636

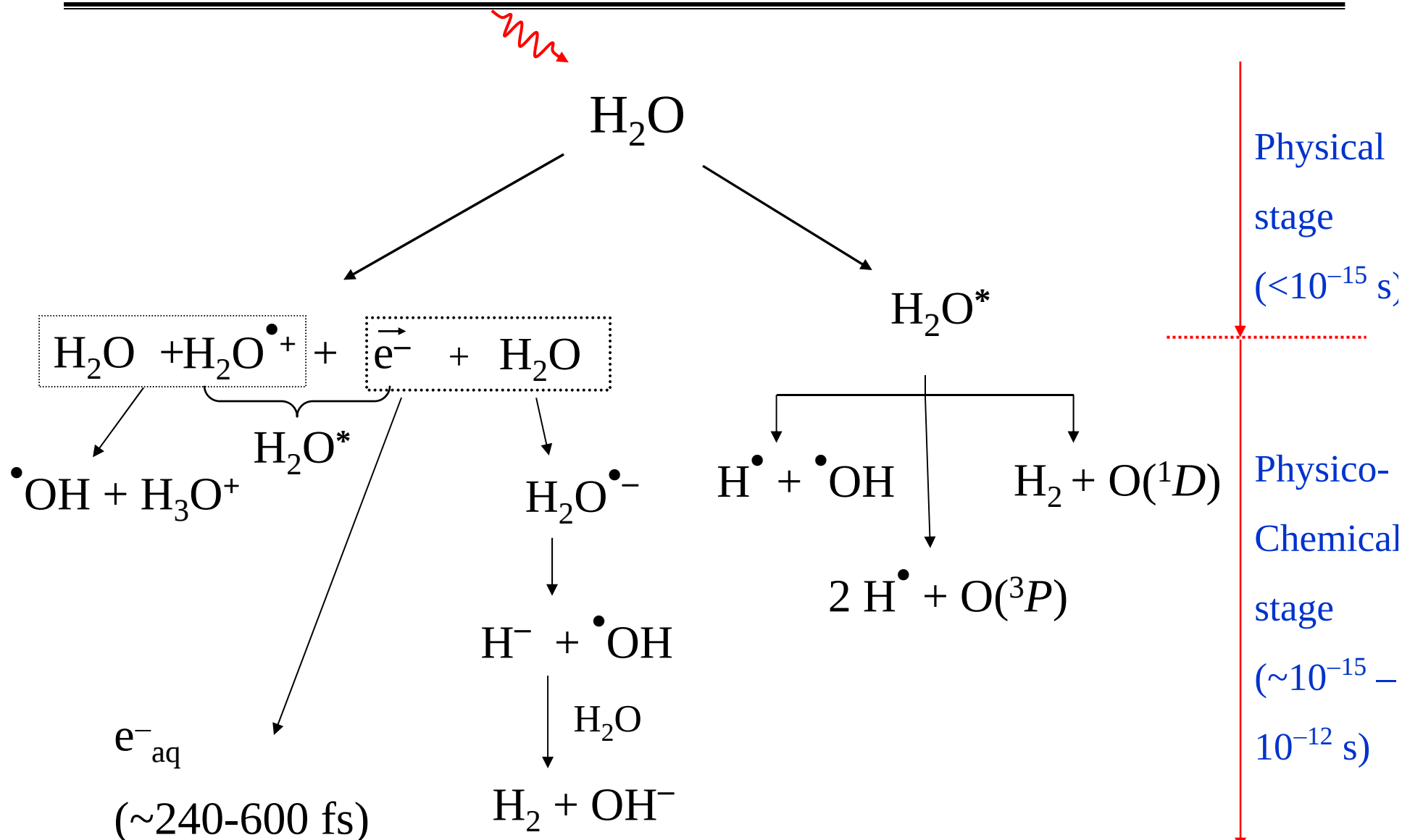


Radiation effects: time sequence of events

Time (s)	Stage	Events	Modeling
10^{-15}	Physical	Energy absorption	Particle transport Cross sections
10^{-12}			
10^{-9}	Chemical	Reorganization	Green's functions
10^{-6}		Electron thermalization	
10^{-3}	Biological	DNA repair	Kinetics models Molecular dynamics



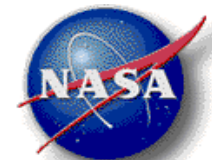
Radiation effects: time sequence of events





Particle transport basics

- ❑ **The trajectory of a particle and all its interactions is followed in the medium**
- ❑ **A particle is followed until**
 - It leaves the volume of interest
 - Its energy decrease below a threshold
 - It disappears by a physical process (e.g. absorption of a photon during a photo-electric effect)
- ❑ **Many other particles are generated by the interactions of the “primary” particle. The trajectories of these secondary particles should also be followed.**

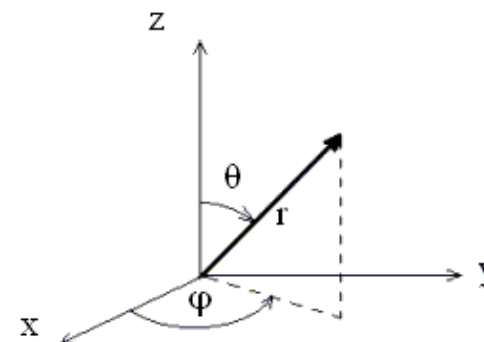


Particle transport basics

□ Particles

- Position (x,y,z)
- Energy (E)
- Direction (θ, φ)

$$\vec{v} = \begin{bmatrix} \sin(\theta) \cos(\varphi) \\ \sin(\theta) \sin(\varphi) \\ \cos(\theta) \end{bmatrix}$$



□ Cross sections

- Probability of interaction between radiation and matter

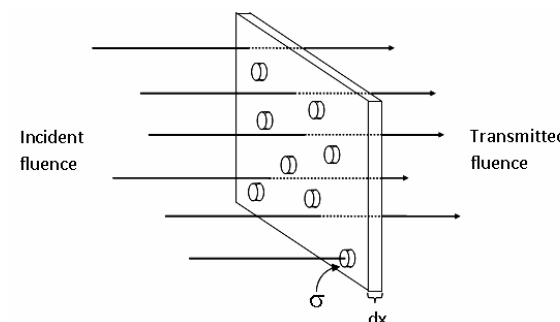
$$dI = -I n \sigma dx$$

I: Incident fluence

n: Density of targets

dx: Width

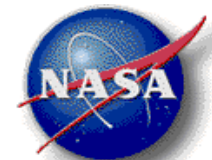
σ : Cross section



- **Cross sections** (units: cm²)
- Mean free path λ (units: cm)

$$I(x) = I(0) \exp(-x / \lambda(E))$$

$$\lambda(E) = 1/(N\sigma(E))$$



Particle transport basics

- ❑ Cross sections (total and differential in energy, angle,... i.e. $d\sigma/dW$, $d\sigma/d\theta$, $d^2\sigma/dWd\sigma$,...) are needed for particle transport
- ❑ The total cross section is the sum of the cross sections for each interactions
- ❑ A distance to the next interaction (s) is sampled from the exponential distribution:

$$s = -\lambda \log(U)$$

$$\lambda(E) = 1/(N\sigma(E))$$

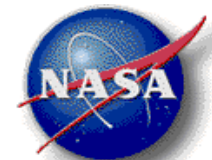
- ❑ The particle is moved to the next interaction site:

$$x' = x + s \sin(\theta) \cos(\varphi)$$

$$y' = y + s \sin(\theta) \sin(\varphi)$$

$$z' = z + s \cos(\theta)$$

- ❑ The interaction (e.g. ionization) is determined by the ratio of the cross section a phenomenon over the total cross section
- ❑ The energy loss and change of direction are determined by sampling the differential cross sections



Cross sections

❑ RITRACKS includes accurate cross section models for all ions and secondary electrons or photons

❑ For electrons:

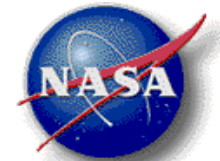
- Ionization
- Excitation
- Elastic collisions
- Dissociative electron attachment
- Bremsstrahlung

❑ For ions:

- Ionization
- Excitation

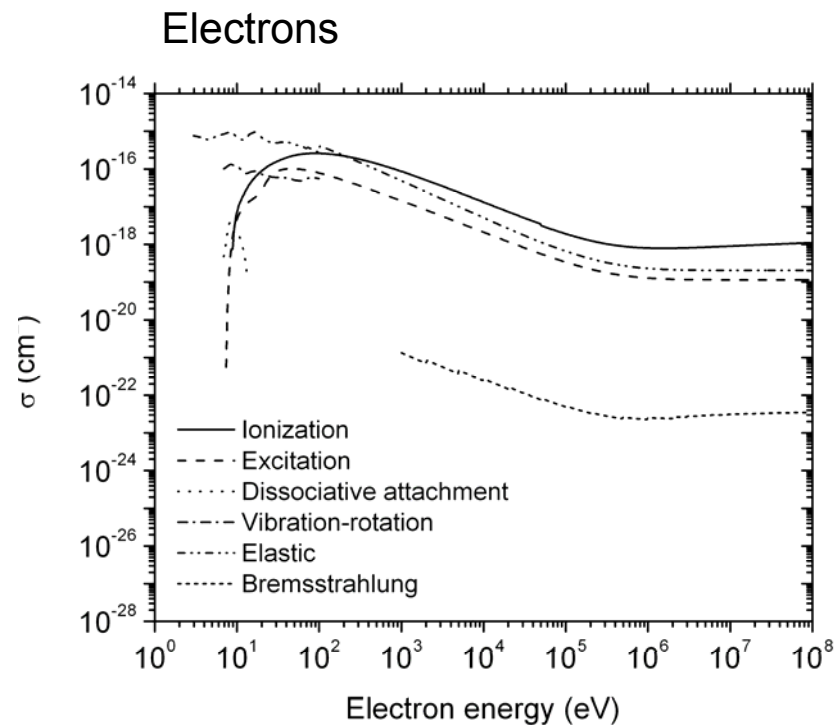
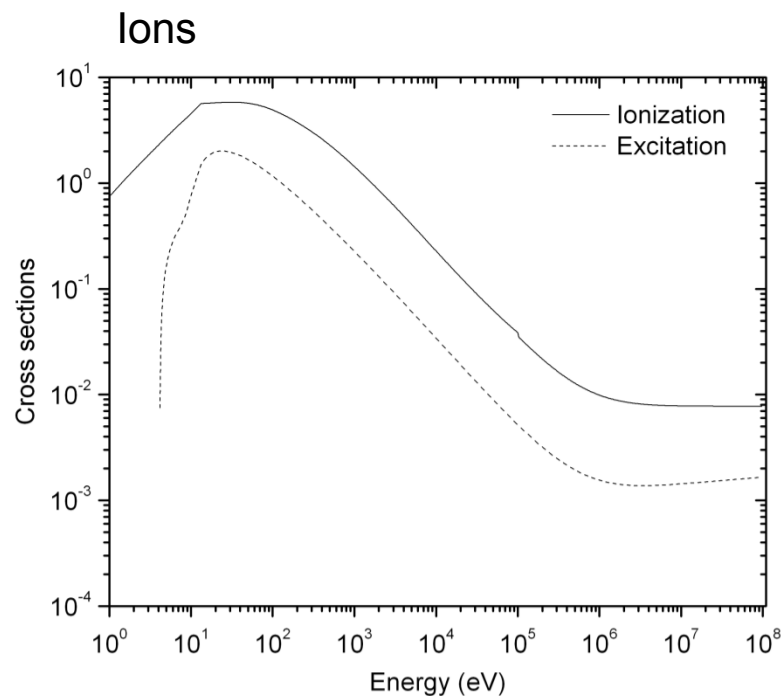
❑ For photons:

- Compton effect
- Coherent diffusion
- Photoelectric effect
- Pair production



Cross sections

□ Cross sections used in RITRACKS



The cross sections for ions are scaled with Z_{eff} :

$$\frac{d\sigma_{\text{ion}}(v)}{dW} = Z_{\text{eff}}^2 \frac{d\sigma_{\text{proton}}(v)}{dW}$$

$$Z_{\text{eff}} / Z = 1 - \exp(-125\beta^2 / Z^{2/3})$$

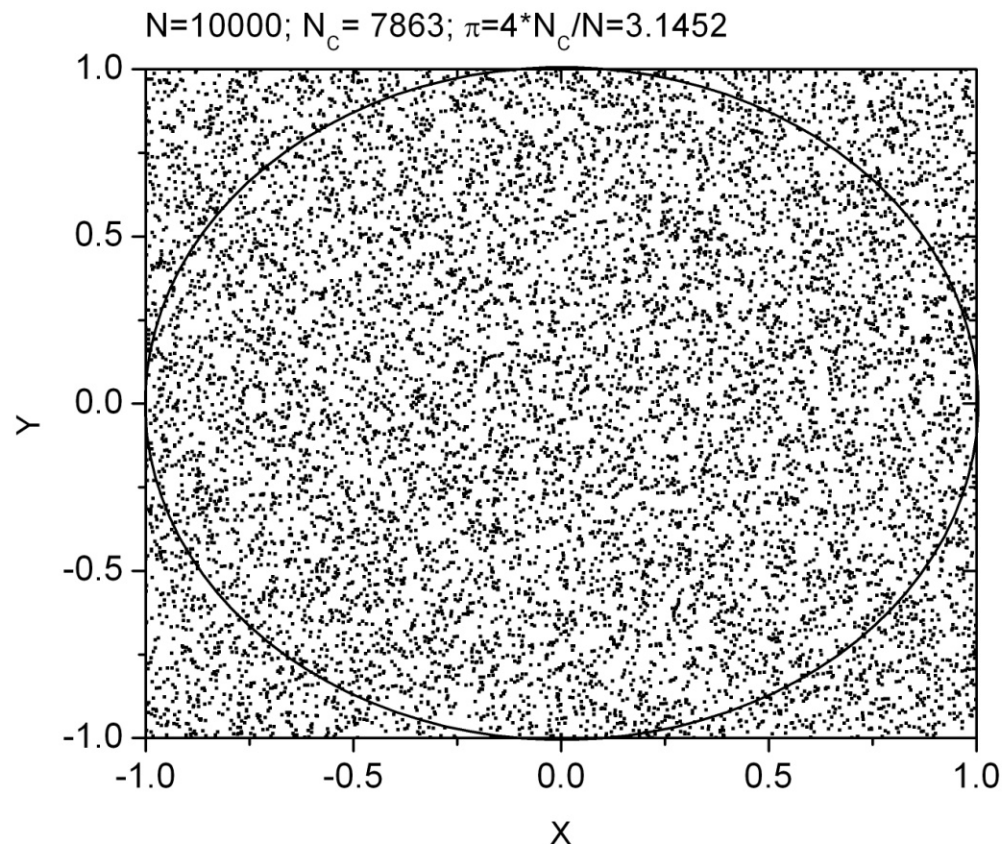
v : velocity of the ion

β : relativistic v/c



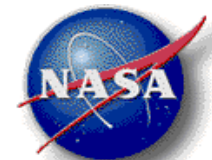
Monte-Carlo simulations

- ❑ Used to simulate stochastic systems



⇒ By increasing the number of random points, $4N_c/N$ converges to the value of π

Example: Calculation of π



Monte-Carlo simulations

- Random numbers
- Probability distributions
- Normalization

$$\sum_{i=1}^N p_i = 1$$

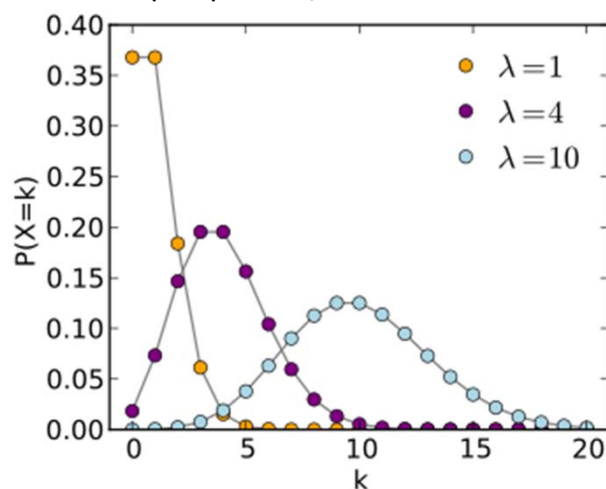
Discrete

$$\int_{-\infty}^{\infty} f(x') dx' = 1$$

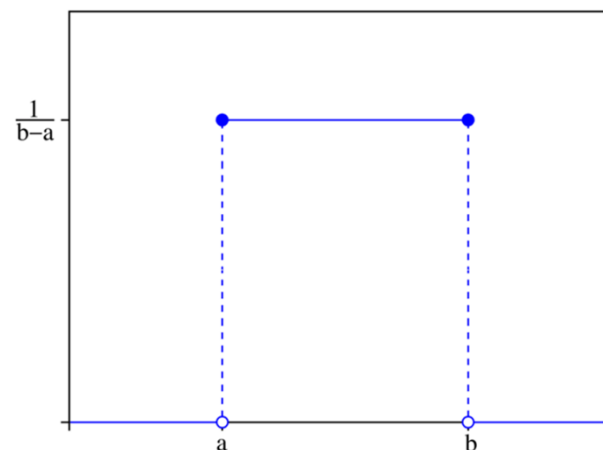
Continuous

Poisson distribution

$$P(x=k) = \lambda^k e^{-\lambda} / k!$$

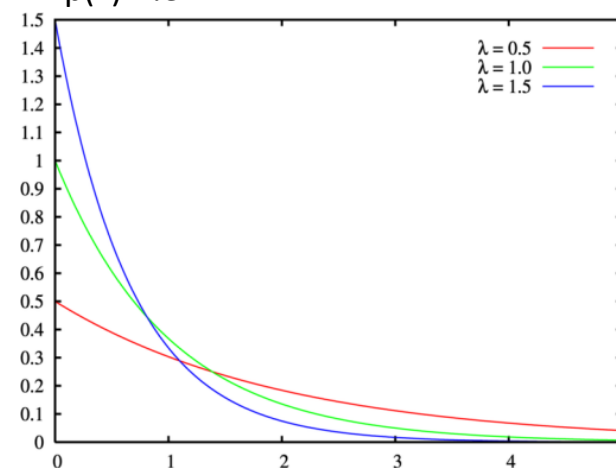


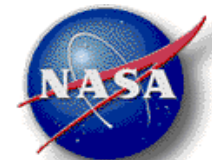
Uniform distribution



Exponential distribution

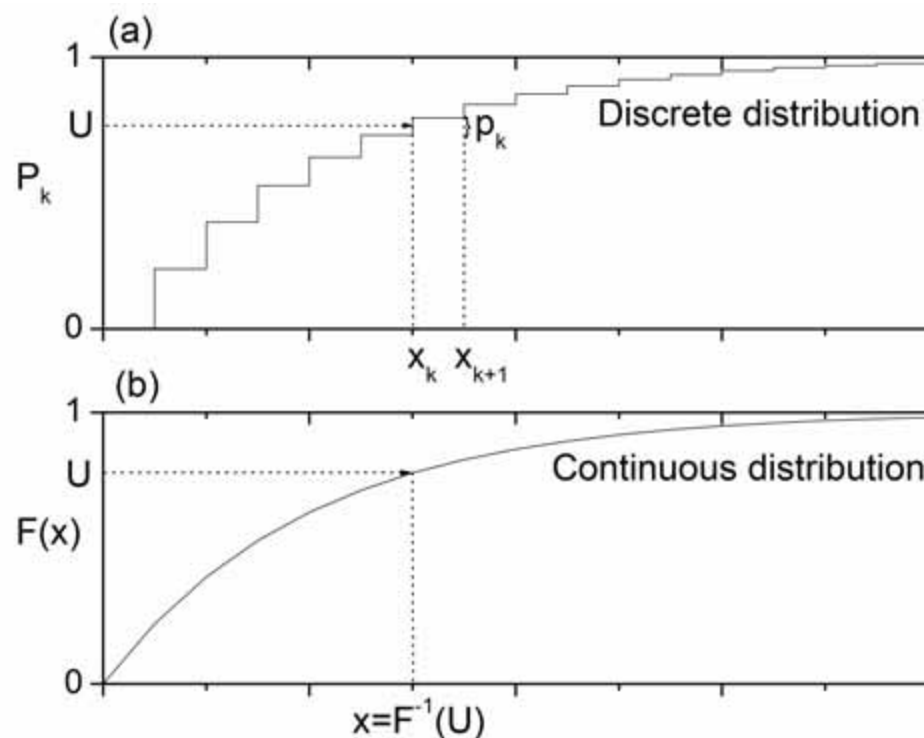
$$p(x) = \lambda e^{-\lambda x}$$





Monte-Carlo simulations

□ Generating probability distributions



Example: Exponential distribution

$$f(x) = \lambda e^{-\lambda x}, \lambda > 0, x \geq 0$$

$$F(x) = 1 - e^{-\lambda x} = U$$

$$X = -\log(1-U)/\lambda \text{ or } X = -\log(U)/\lambda$$

U is a random number between 0 and 1

F(x) is the cumulative probability distribution

$$F(x) = \int_{-\infty}^x f(x') dx'$$

$$P_k = \sum_{i=1}^k p_i$$

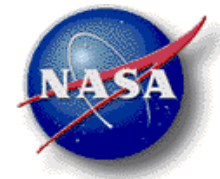


The software RITRACKS

❑ The software RITRACKS comprises several parts

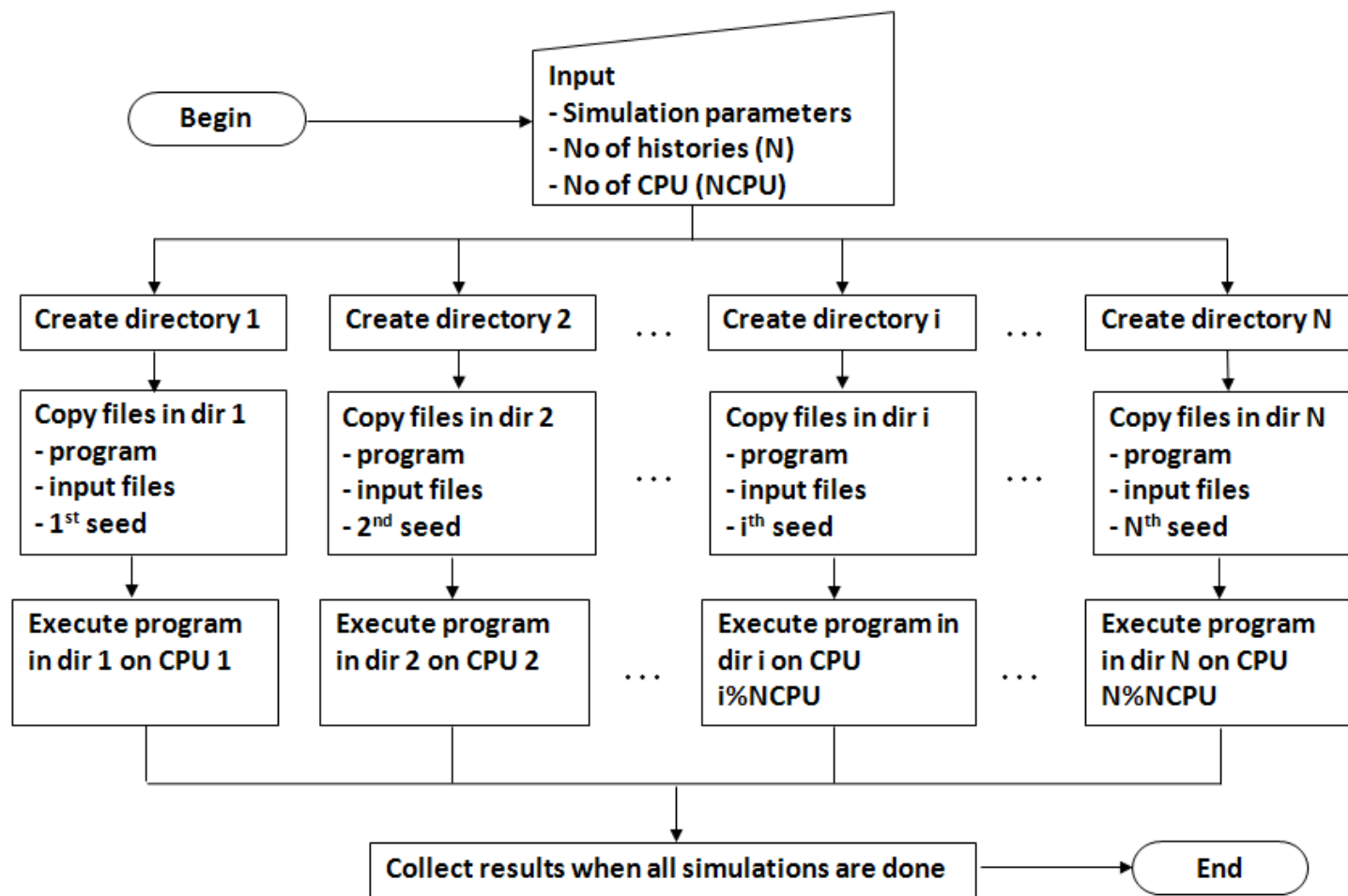
- The calculation part includes:
 - ✓ The cross sections, which are necessary for particle transport
 - ✓ The particle transport routines
 - ✓ Post-simulation data management
- The Graphic User Interface (GUI), comprises several windows:
 - ✓ The main window
 - ✓ Incident radiation window
 - ✓ Cross sections windows (electrons and ions)
 - ✓ Results (events) details
- The 3D visualization window
- The help file

❑ All necessary files are included in an installer for Windows



The software RITRACKS

❑ Multiple CPU computing

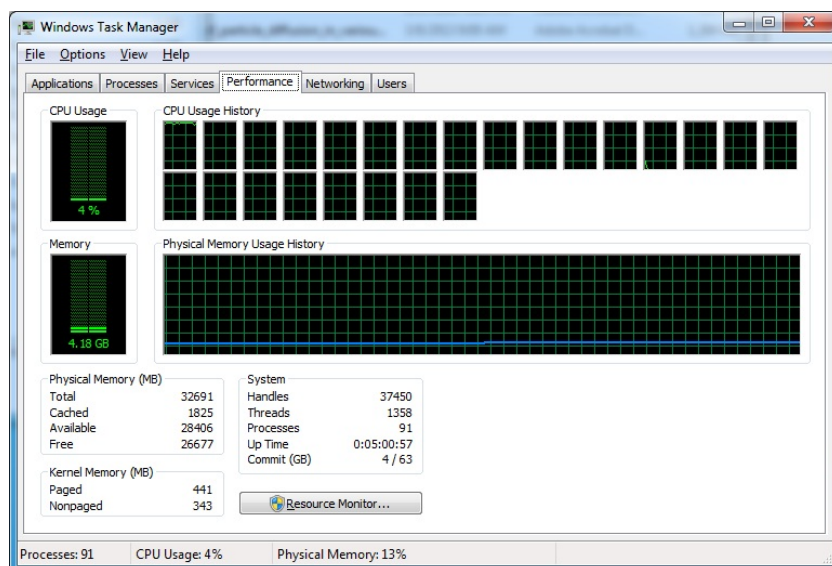




The software RITRACKS

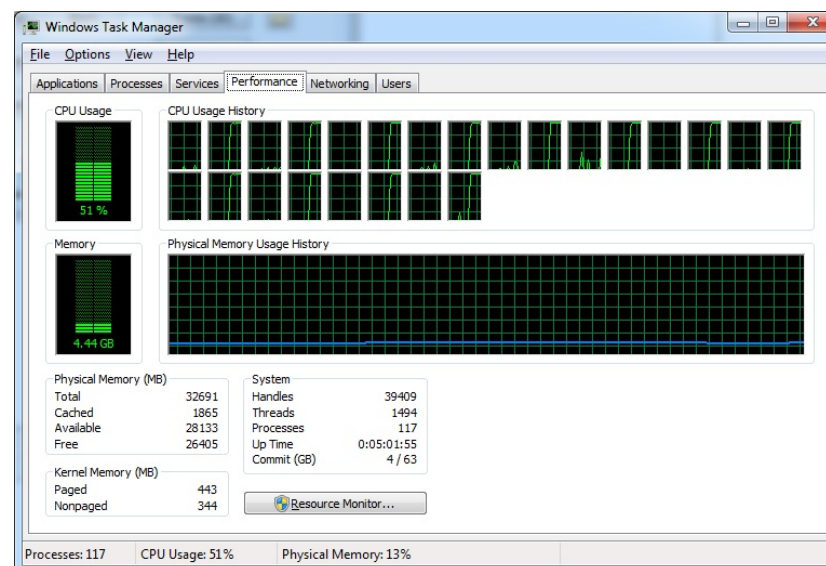
❑ Multiple CPU computing (Windows)

RITRACKS V1



Use one CPU only

RITRACKS V3

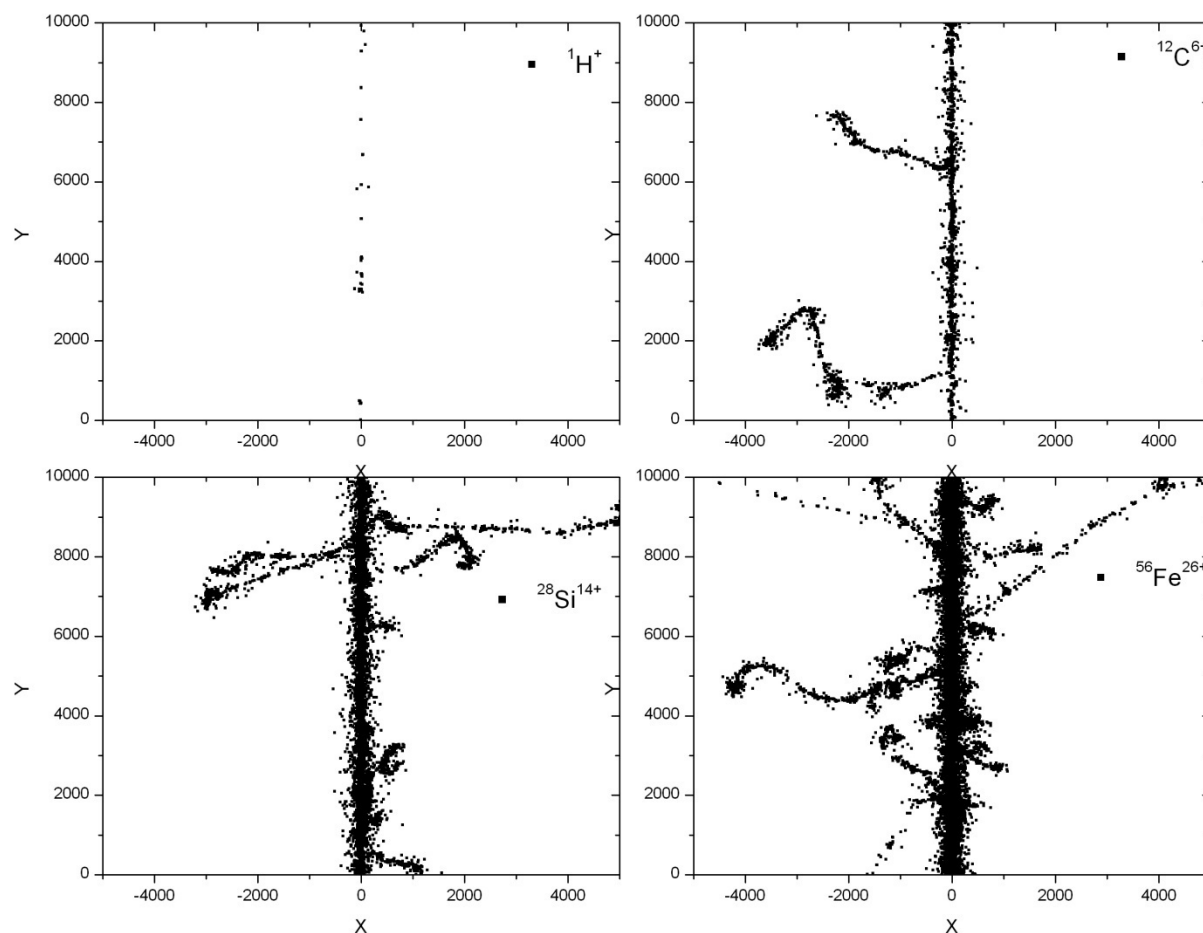


Choose the CPUs you want to use



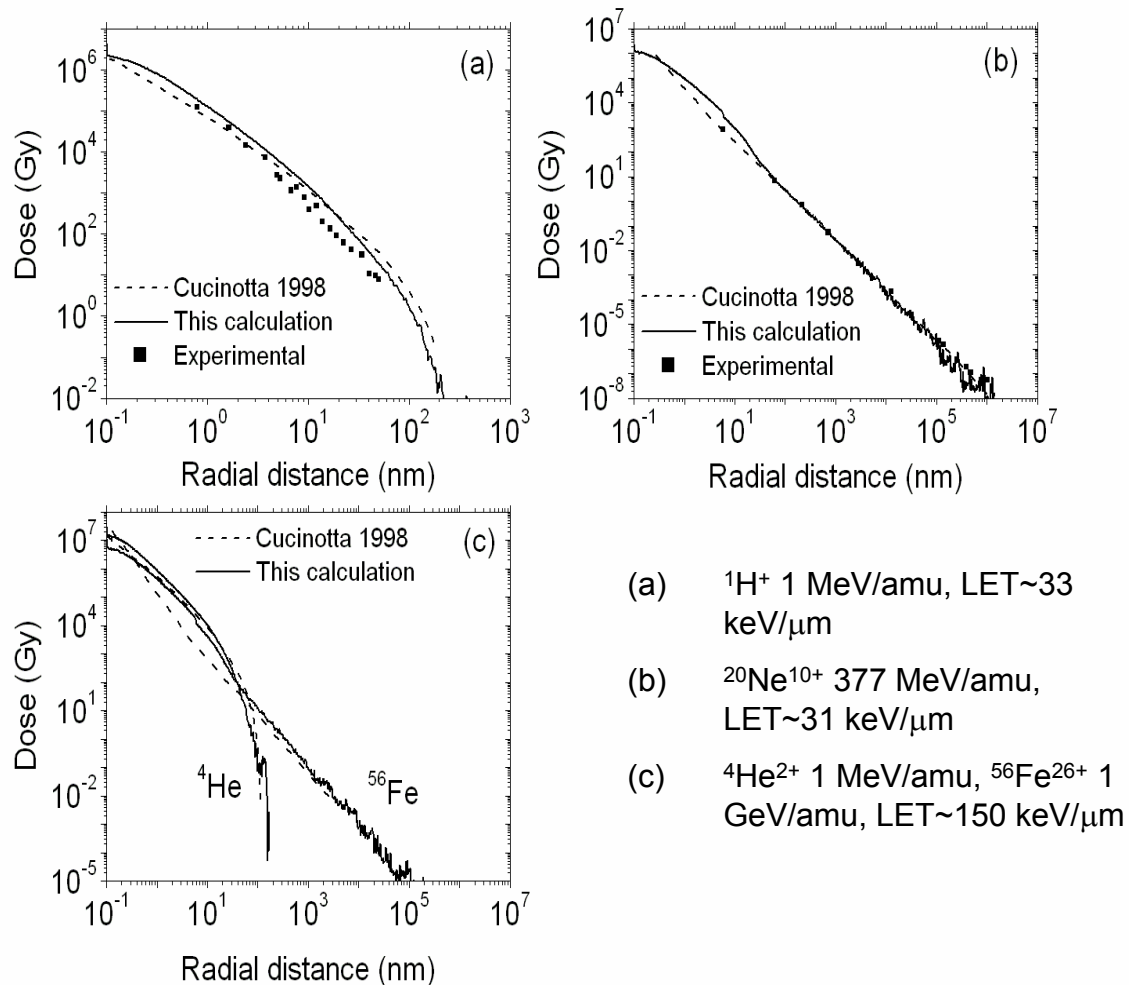
Heavy ion track structure simulation

Simulation for $^1\text{H}^+$, $^{12}\text{C}^{6+}$, $^{28}\text{Si}^{14+}$ and $^{56}\text{Fe}^{26+}$ tracks, 100 MeV/amu



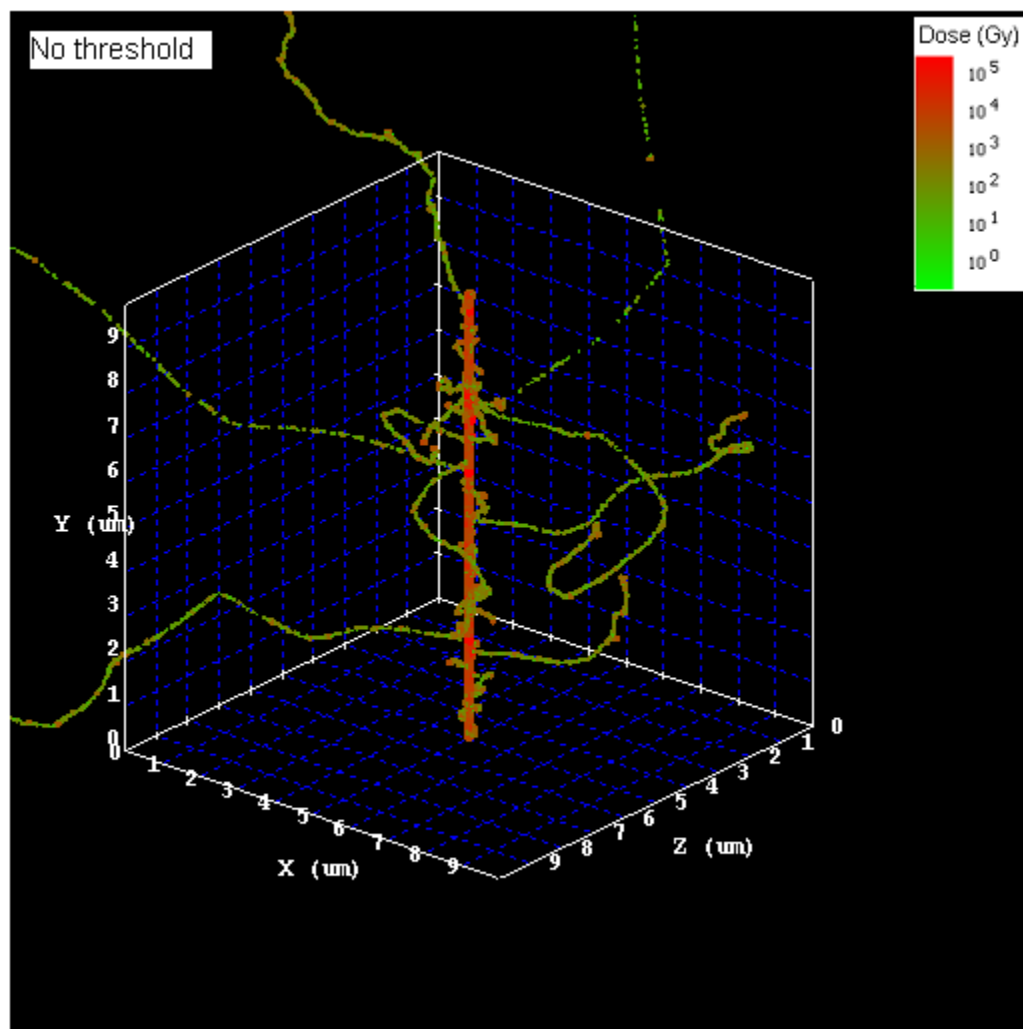


Radial dosimetry





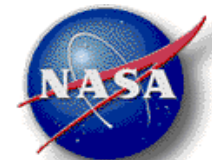
Voxel dosimetry



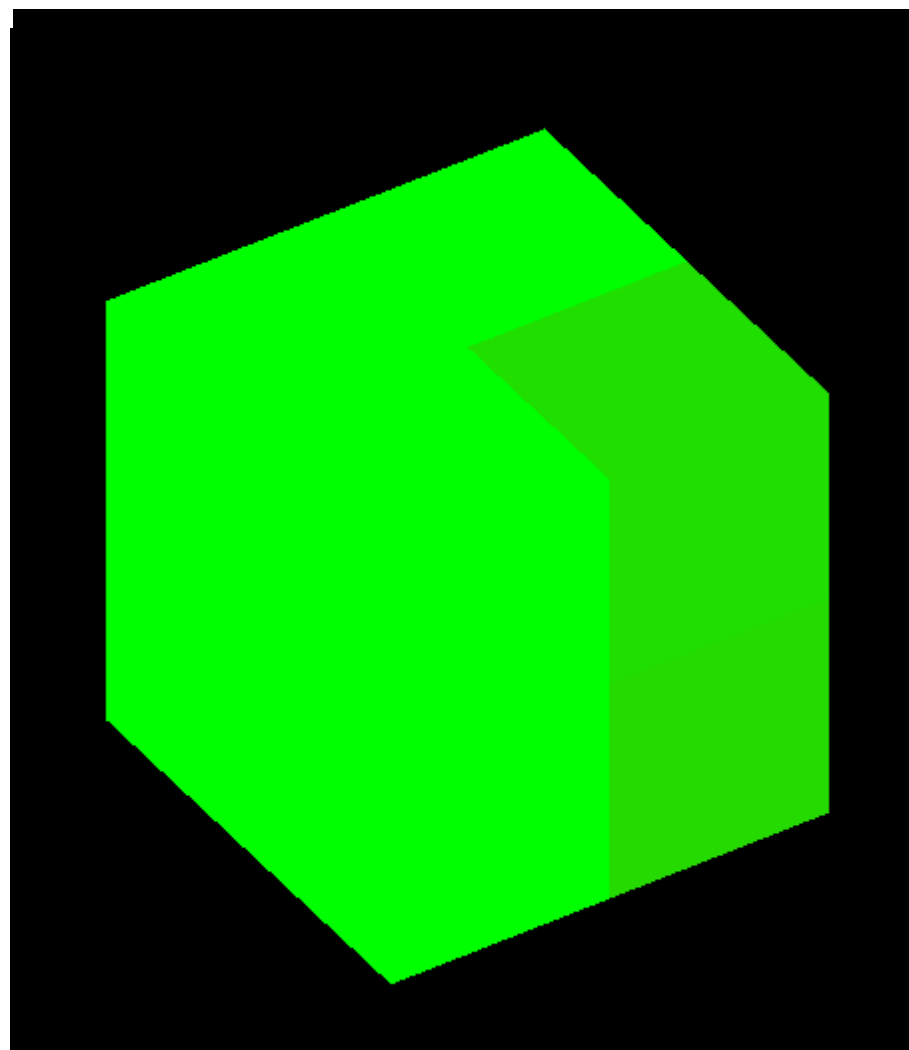
1 GeV/amu $^{56}\text{Fe}^{26+}$ ion

LET~150 keV/μm

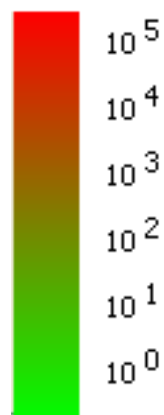
Voxels: 40 nm x 40 nm x 40 nm



Voxel dosimetry

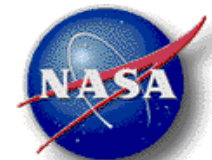


Dose (Gy)

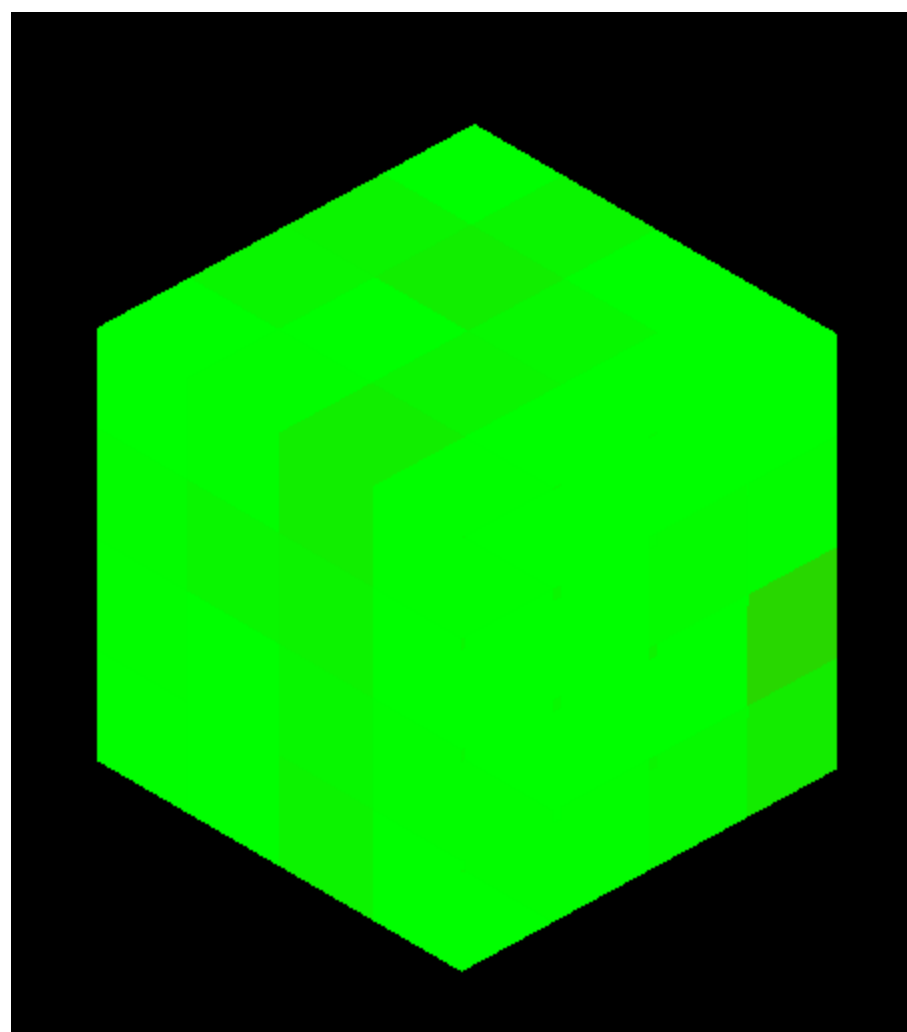


- ☐ Calculations with RITRACKS
- ☐ 1 $^{56}\text{Fe}^{26+}$ ions, 1 GeV/amu
- ☐ LET: ~ 150 keV/ μm
- ☐ Irradiated volume: $5 \mu\text{m} \times 5 \mu\text{m} \times 5 \mu\text{m}$
- ☐ Voxels: 20 nm, 40 nm, 80 nm, 160, 320 nm, 640 nm, 1280 nm, 2560 nm

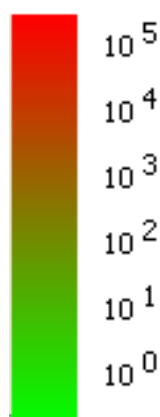
Voxels size: 2560 nm



Voxel dosimetry

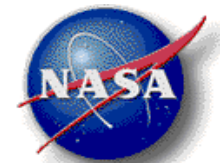


Dose (Gy)



- ☐ Calculations with RITRACKS
- ☐ 450 $^1\text{H}^+$ ions, 300 MeV
- ☐ LET: $\sim 0.3 \text{ keV}/\mu\text{m}$
- ☐ Irradiated volume: $5 \mu\text{m} \times 5 \mu\text{m} \times 5 \mu\text{m}$
- ☐ Voxels: 20 nm, 40 nm, 80 nm, 160 nm, 320 nm, 640 nm, 1280 nm

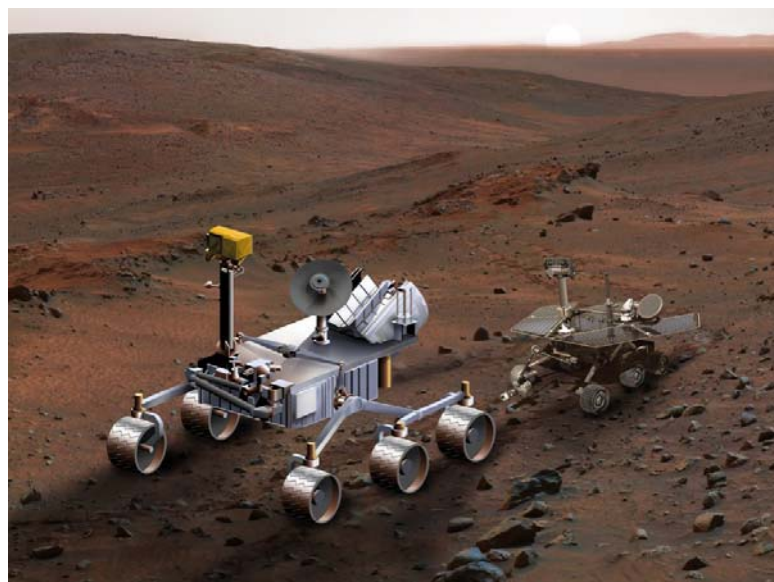
Voxels size: 1280 nm



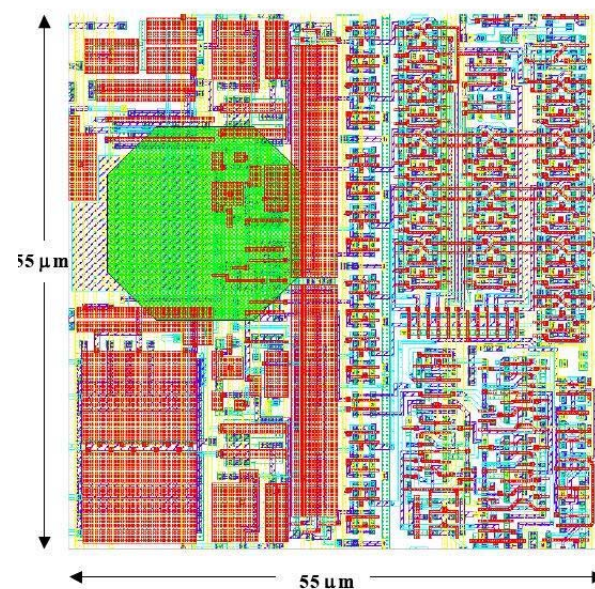
Space radiation detectors

- ❑ RITracks may be used to simulate ISS and Mars Science Laboratory (MSL) detectors

RAD Detector on MSL
(particle and neutron spectrometer)



ISS MEDIPIX
Current Medipix2 Cell Layout



503 transistors
per pixel

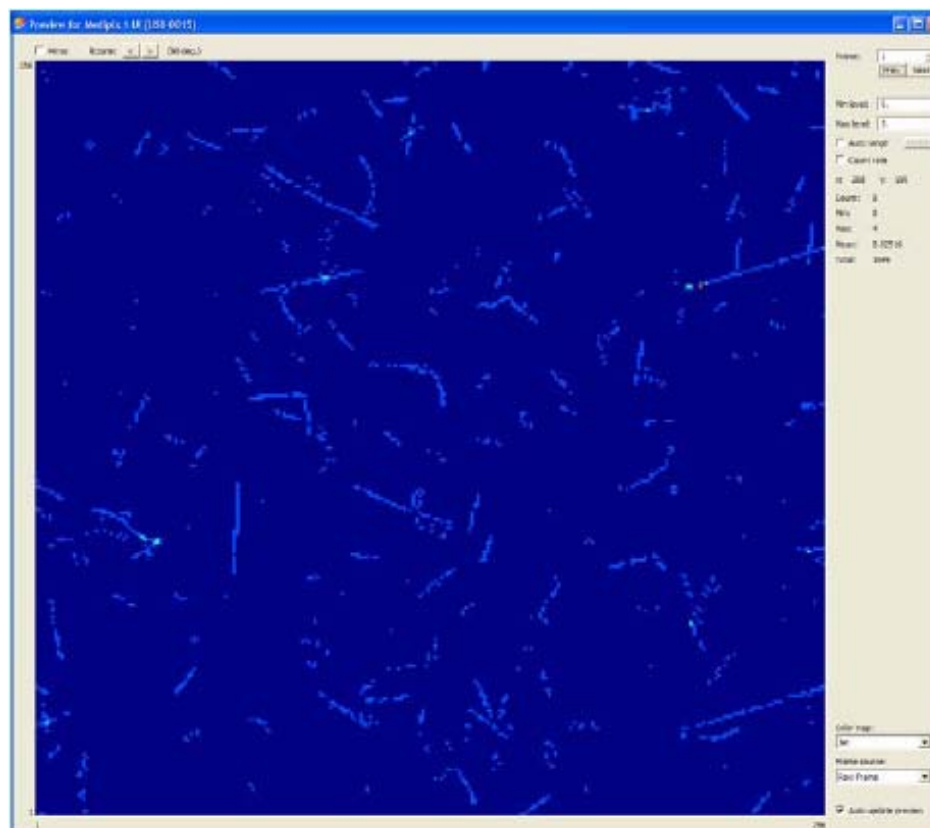
33M per Chip



Space radiation detectors



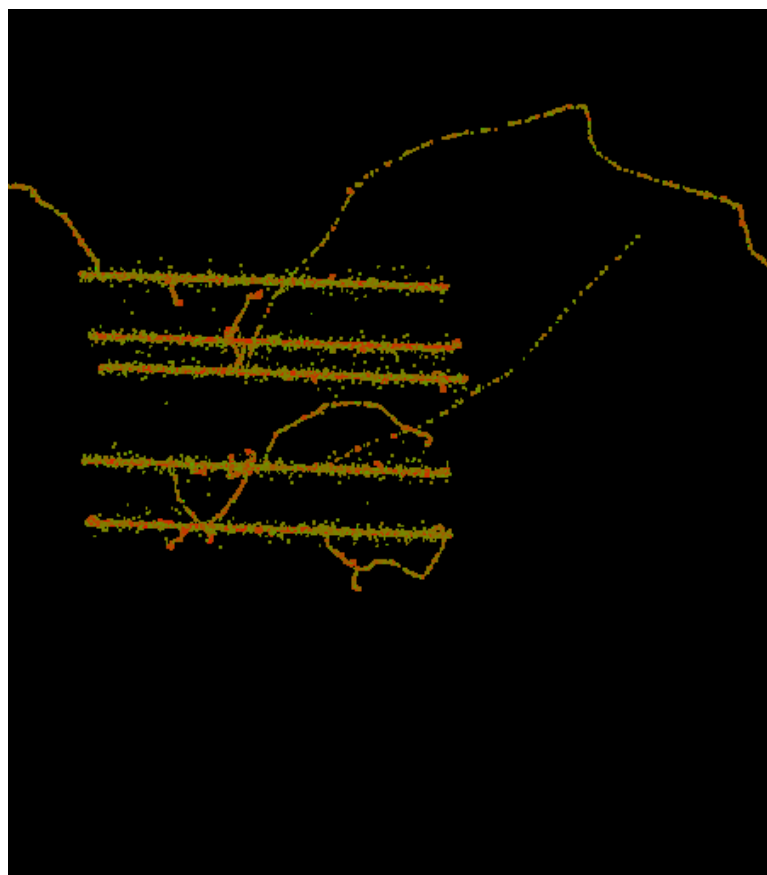
Electrons, 50000 eV
Area: $100\ \mu\text{m} \times 100\ \mu\text{m}$
Voxels: $1\ \mu\text{m} \times 1\ \mu\text{m} \times 1\ \mu\text{m}$



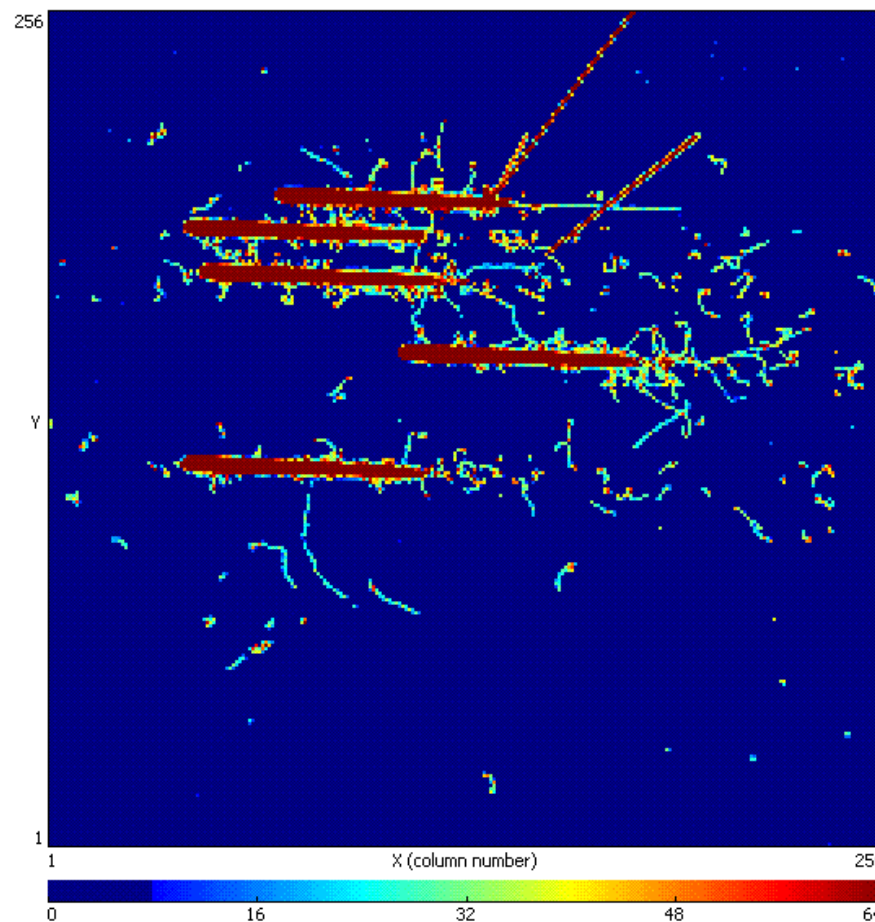
Medipix2 images obtained In a 777 airliner at 34,000 feet over Anchorage, Alaska on a flight to Japan...



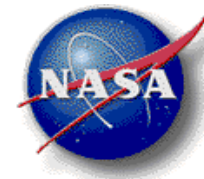
Space radiation detectors



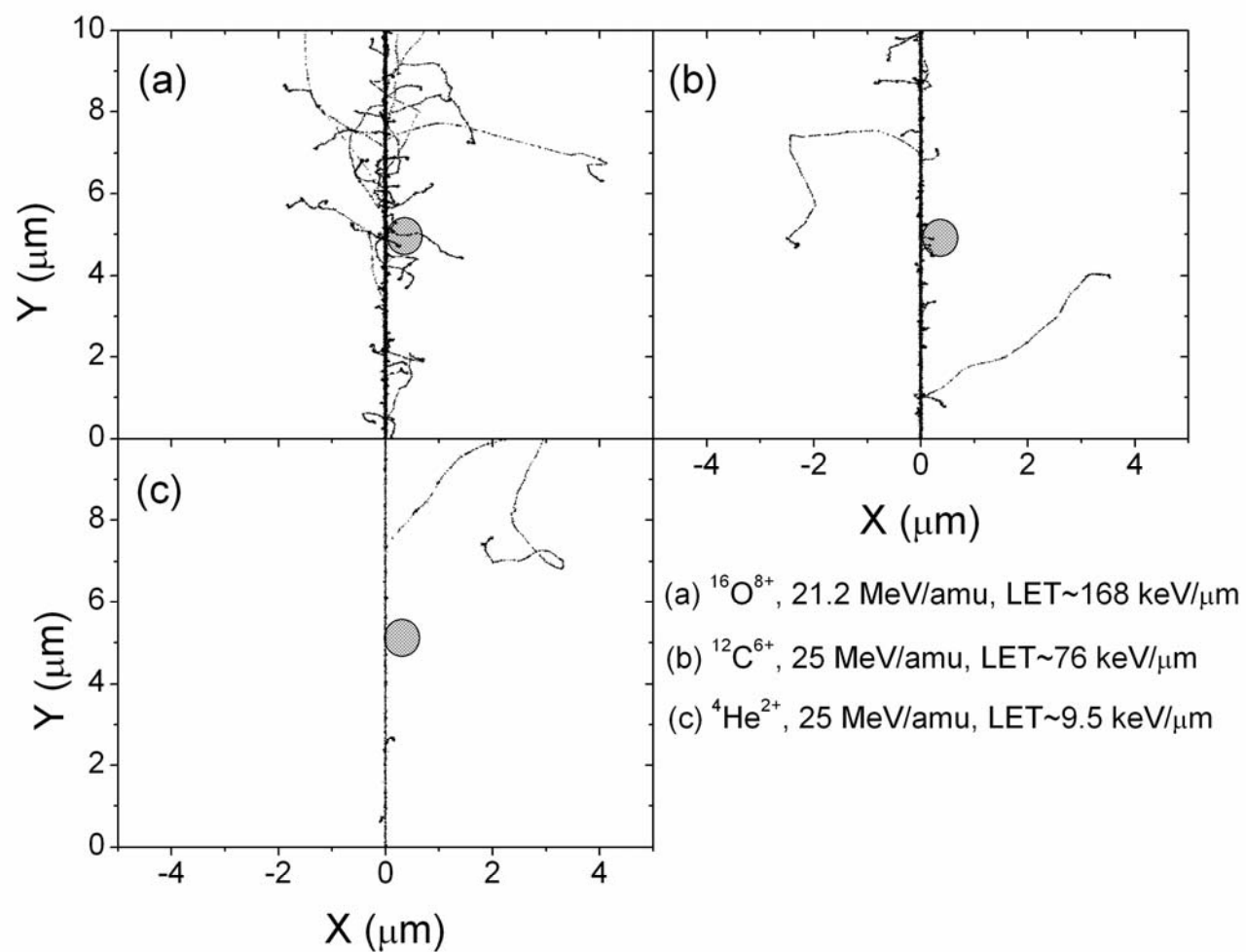
Si ions, 800 MeV/u
Area: 5 μm x 5 μm
Voxels: 20 nm x 20 nm x 20 nm

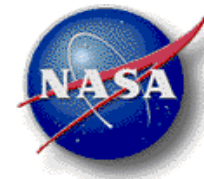


Medipix2 images obtained for 800 MeV/u Si ions

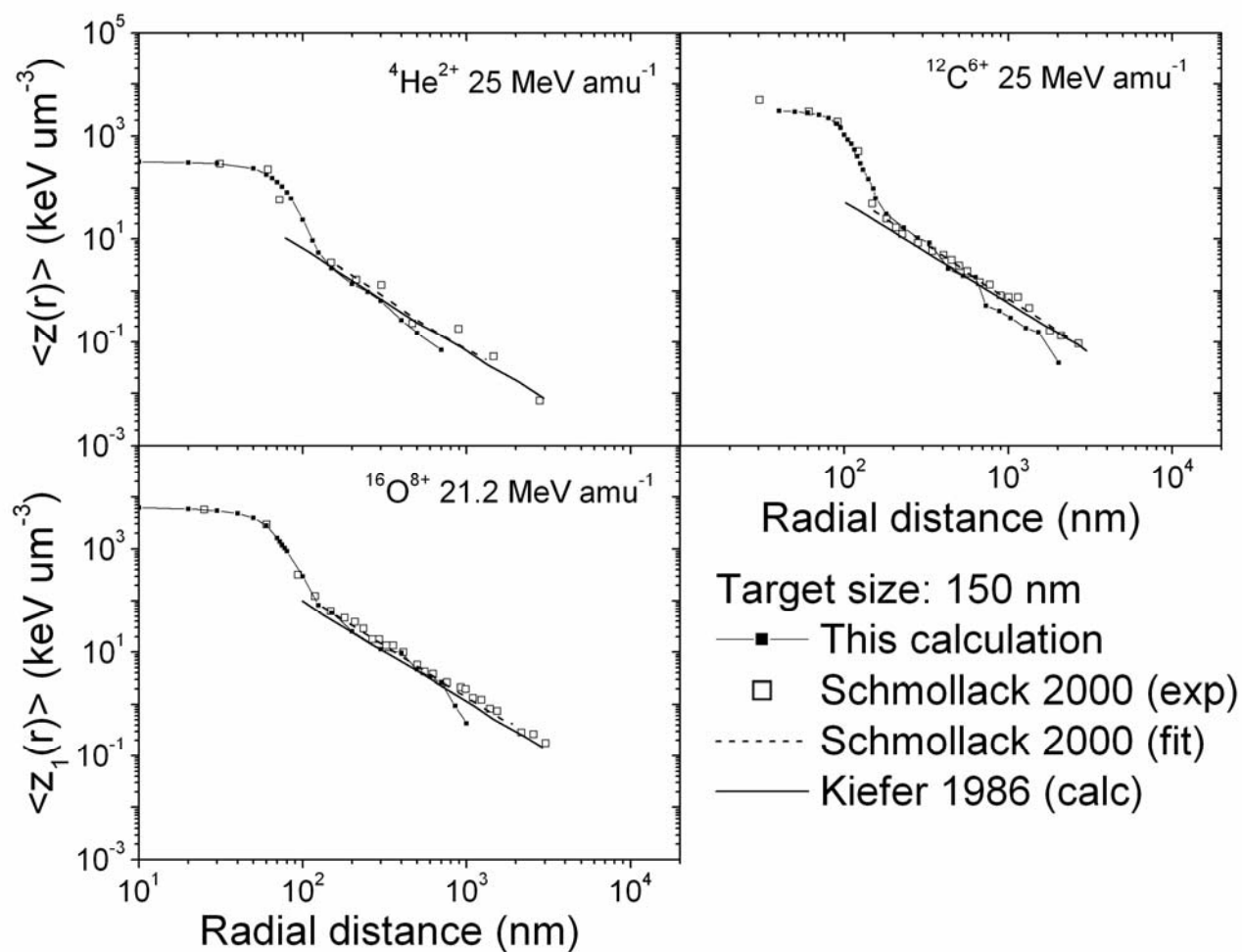


Target dosimetry





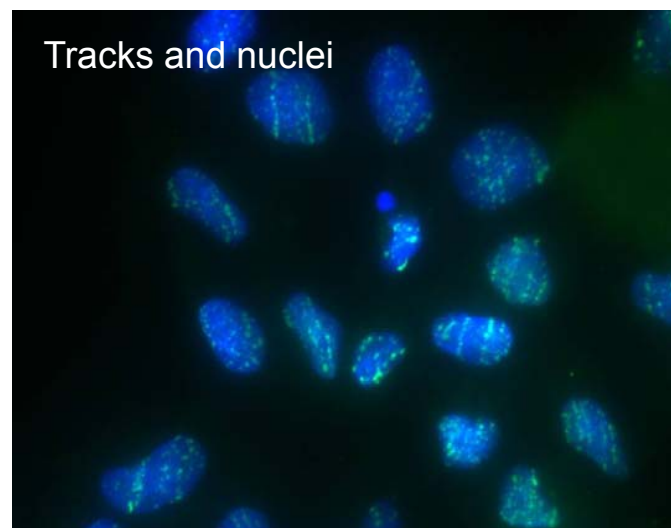
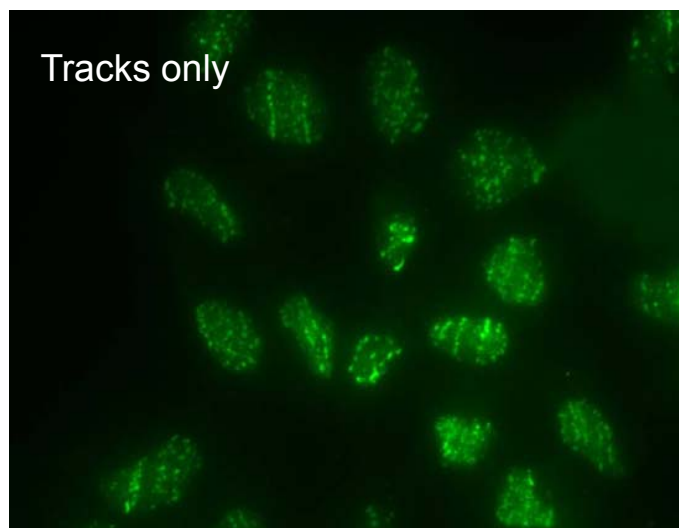
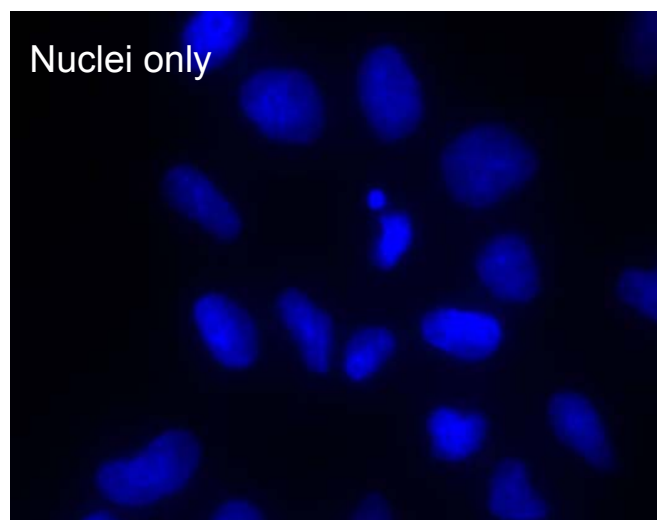
Target dosimetry





DNA damage / γ H2AX foci studies

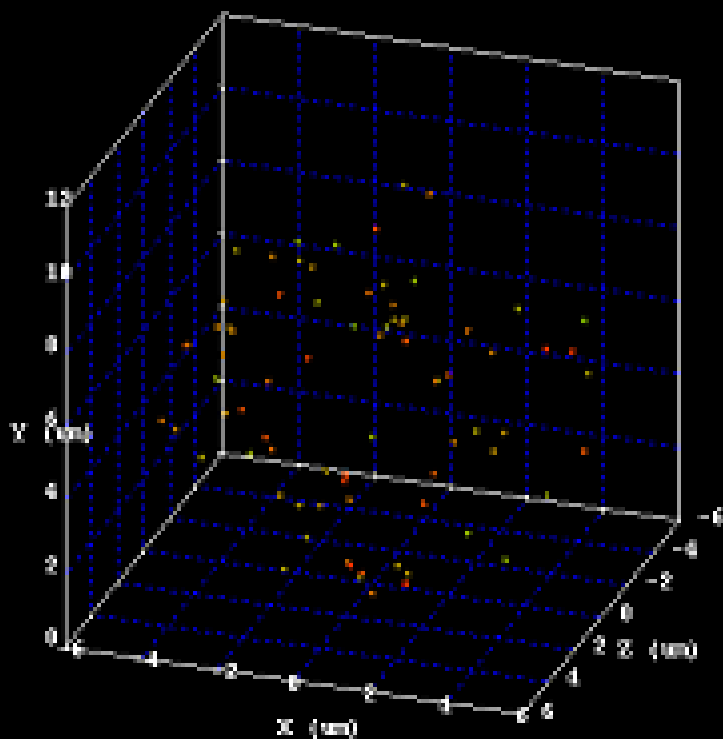
- Irradiation by 1 GeV/amu Fe ions
- 100 cGy
- LET ~ 149 keV/ μ m





DNA damage

Calculated DSB



2700 x $^1\text{H}^+$, 300 MeV (1 Gy)

Dose in voxels (20 nm)

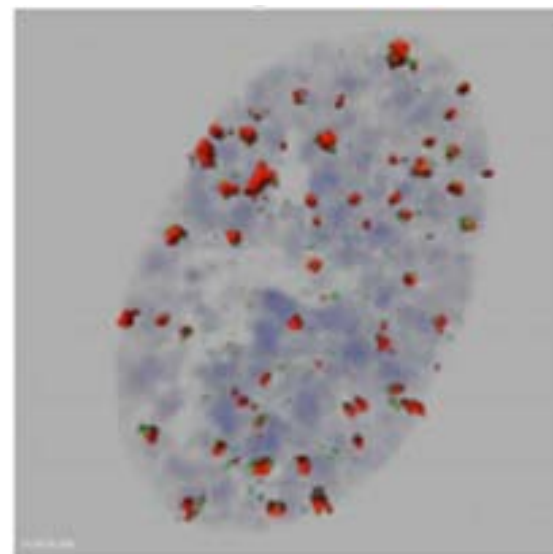
Chromosomes (RW model)

Intersection voxels

H2AX foci experiments

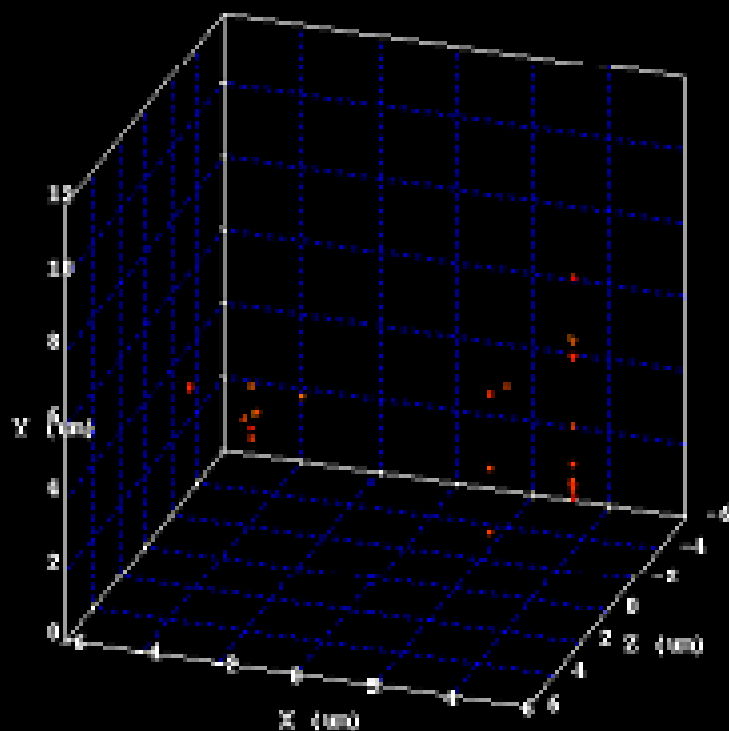
Application of DSB probability

$$\psi = 1 - e^{-QD(t)}$$



DNA damage

Calculated DSB



$6 \times {}^{56}\text{Fe}^{26+}$, 1 GeV/u (1 Gy)

Dose in voxels (20 nm)

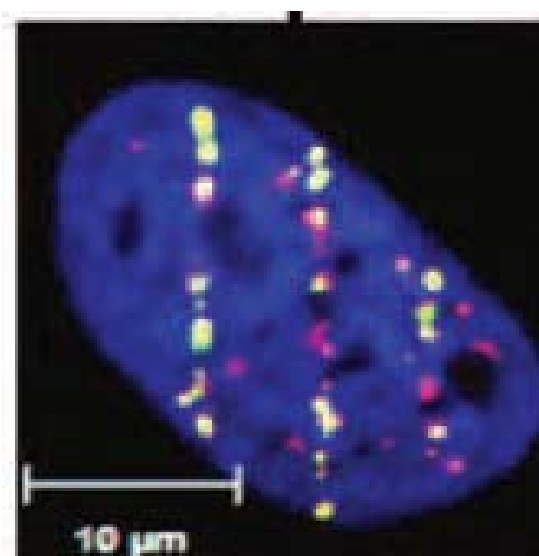
Chromosomes (RW model)

Intersection voxels

H2AX foci experiments

Application of DSB probability

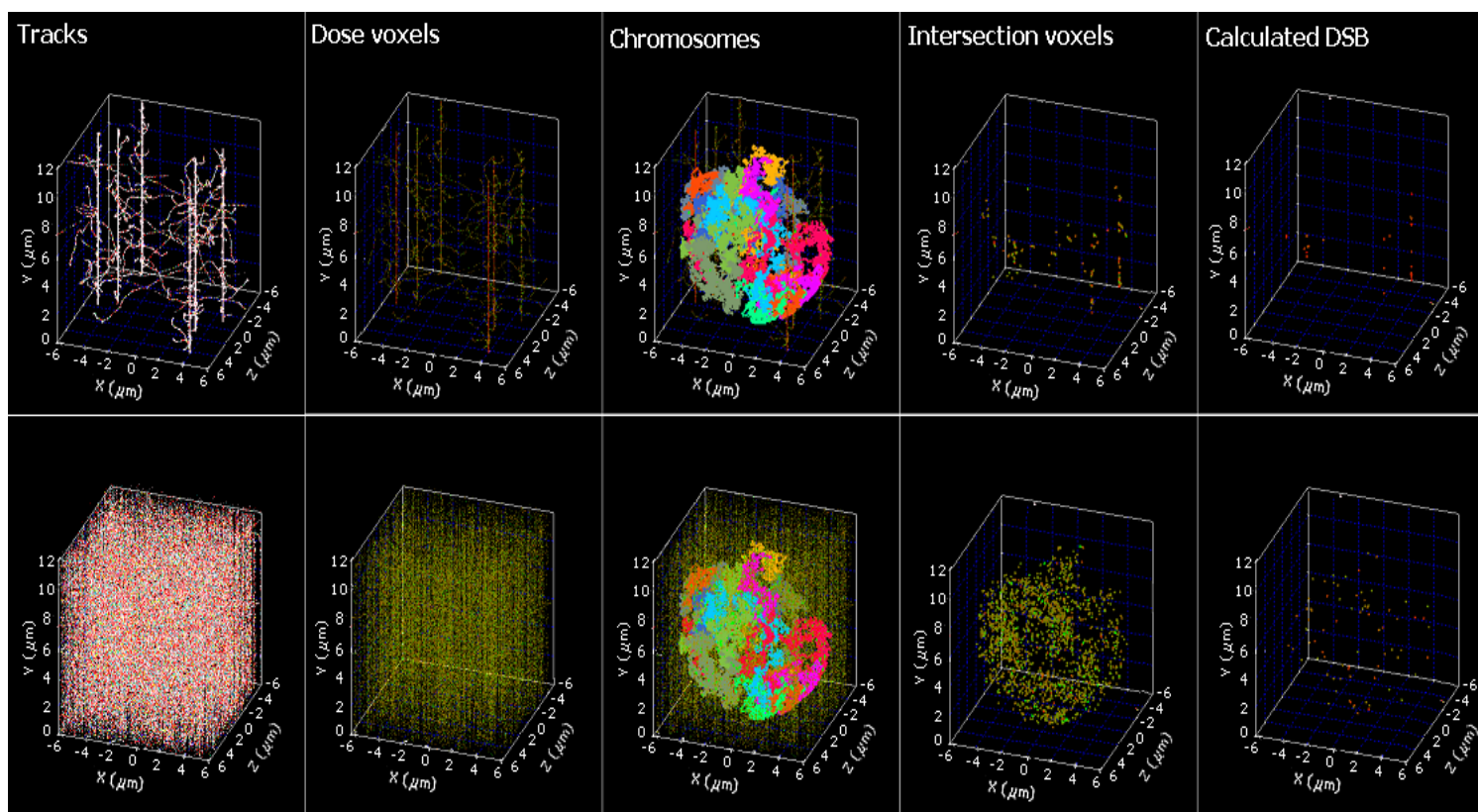
$$\psi = 1 - e^{-QD(t)}$$





DNA damage / γ H2AX foci studies

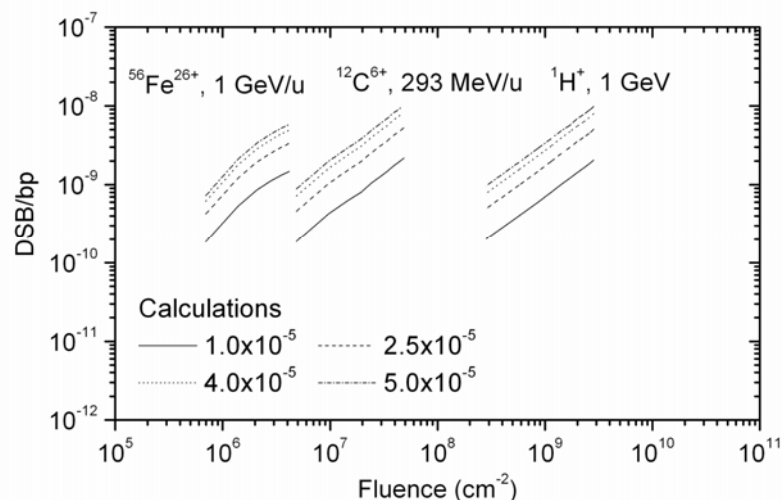
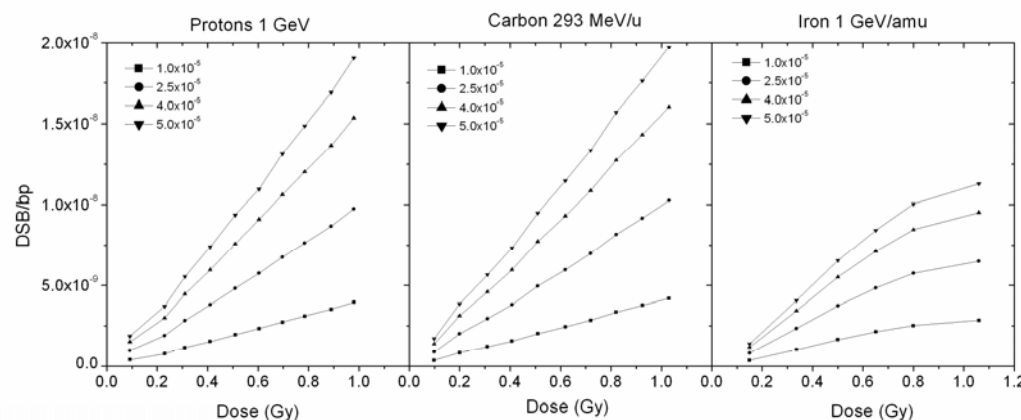
- Calculation of DSBs by low- and high-LET radiation





DNA damage / γ H2AX foci studies

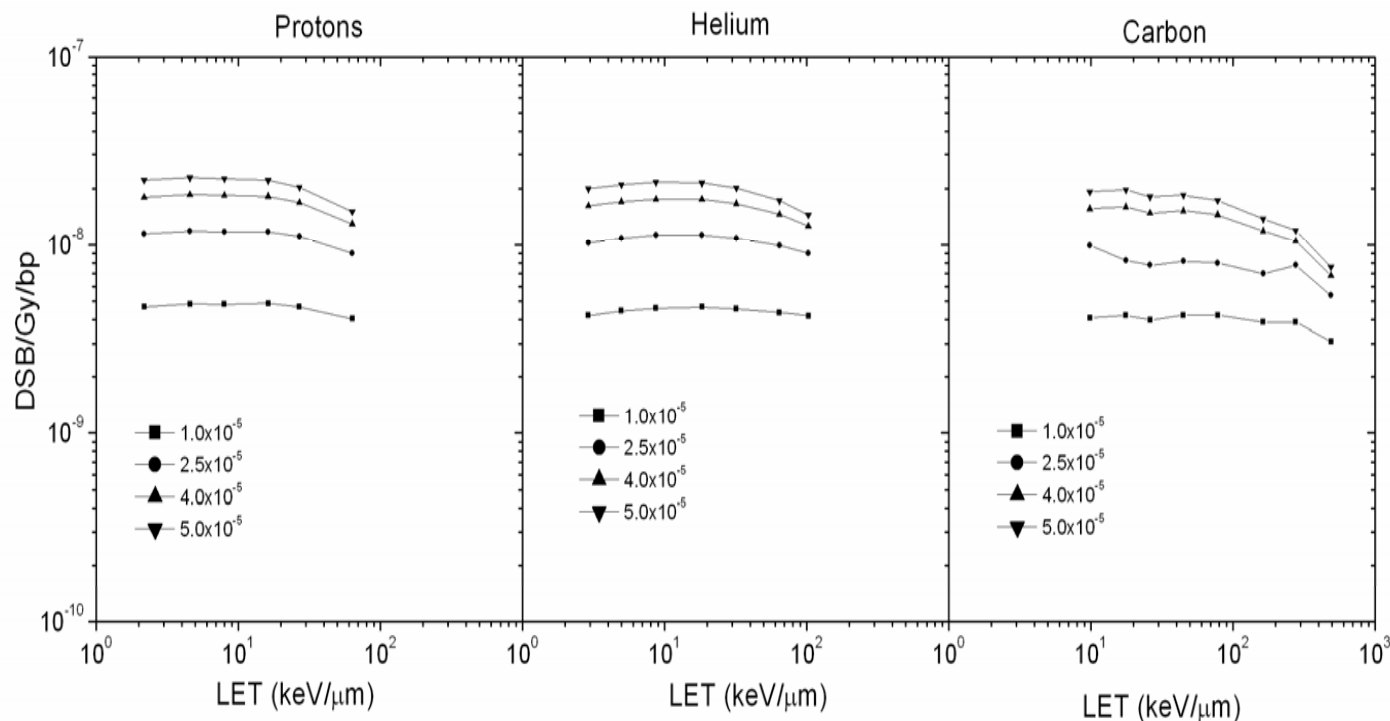
- Calculation of DSBs by $^1\text{H}^+$, $^{12}\text{C}^{6+}$ and $^{56}\text{Fe}^{26+}$ ions

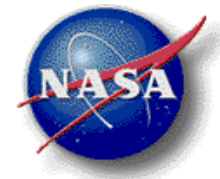




DNA damage / γ H2AX foci studies

- Calculation of DSBs vs LET by $^1\text{H}^+$, $^{12}\text{C}^{6+}$ and $^{56}\text{Fe}^{26+}$ ions

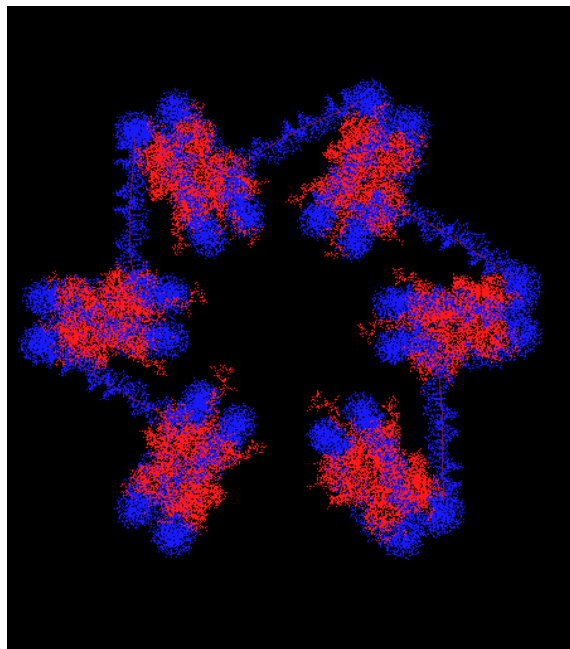




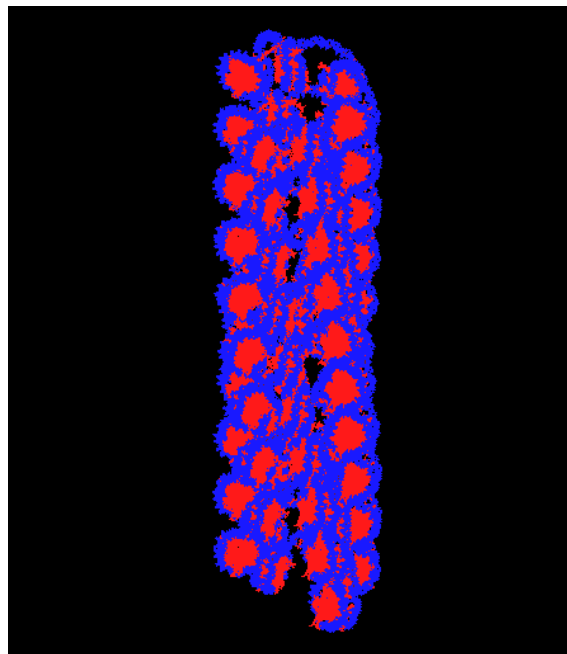
DNA damage simulations

- ❑ To better understand the formation of DSBs, a chromatin fiber is build from nucleosome units and linker DNA

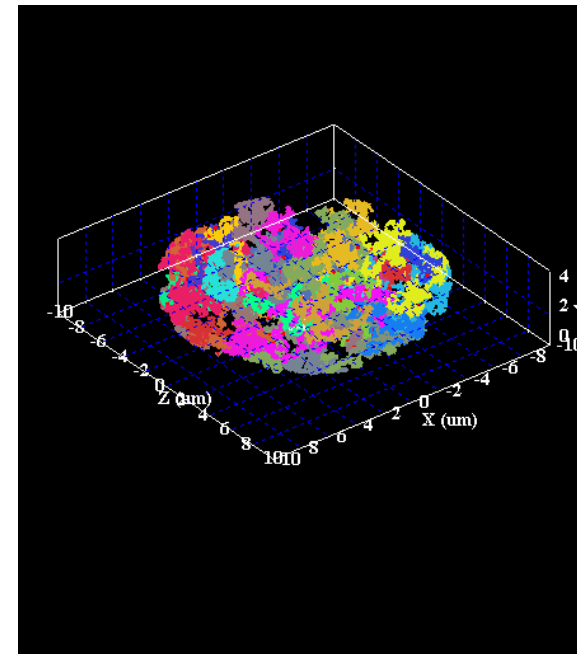
Nucleosome (DNA fragments)



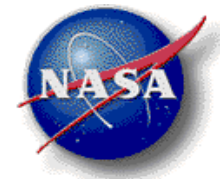
Chromatin fiber



Nuclei



Nuclei simulations courtesy of Dr. Artem Ponomarev



DNA damage simulations

❑ The Binary-Encounter-Bethe (BEB) model of ionization cross section

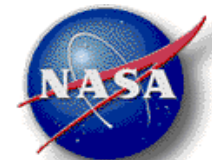
$$\frac{d\sigma}{dw} = \frac{s}{t+u+1} \left\{ \frac{1}{(t-w)^2} + \frac{1}{(1+w)^2} - \frac{1}{1+t} \left[\frac{1}{t-w} + \frac{1}{1+w} \right] + \left[\frac{1}{(t-w)^3} + \frac{1}{(1+w)^3} \right] \log(t) \right\}$$

❑ The energies are expressed in units of ionization potential of the orbital (B):

- $t=T/B$ is the kinetic energy of the incident electron
- $w=W/B$ is the kinetic energy of the ejected electron
- $u=U/B$ is the kinetic energy of the electron in the orbital

❑ The total cross section is obtained by integration

$$\sigma = \int_0^{(t-1)/2} \frac{d\sigma}{dw} dw = \frac{s}{t+u+1} \left\{ 1 - \frac{1}{t} + \frac{1}{2} \left[1 - \frac{1}{t^2} \right] \log(t) - \frac{\log(t)}{t+1} \right\}$$

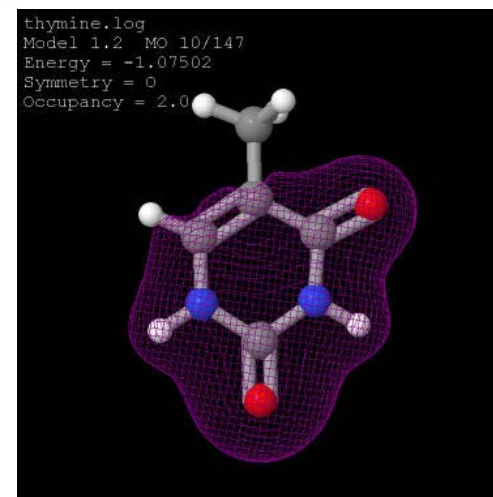
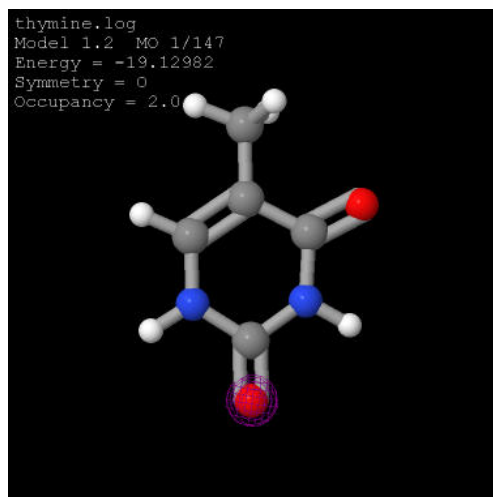
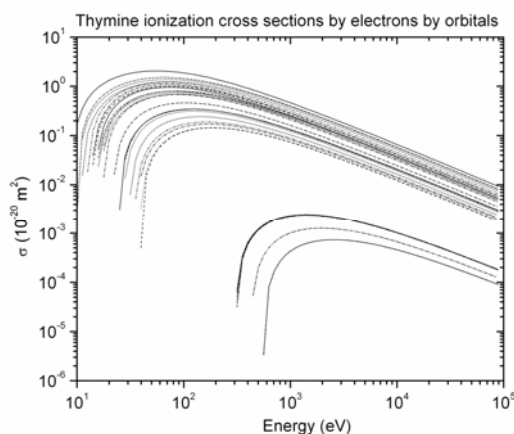


DNA damage simulations

- ❑ In the DNA bases, there are many internal and valence electrons. The BEB model allows to model the ionization for each electron of the molecule.

Thymine

	No	U (eV)	B (eV)	N
Internal electrons (18)	1	794.1	559.41	2
	2	794.1	559.18	2
	3	601.5	425.6	2
	4	601.5	425.48	2
	5	435.9	311.36	2
	6	435.9	310.43	2
	7	435.8	308	2
	8	435.7	306.41	2
	9	435.8	305.8	2
Valence electrons (44)	10	66.26	40.06	2
	11	71.74	39.14	2.04
	12	63.05	36.16	1.86
	13	57.89	34.56	1.85
	14	44.95	30	2.3
	15	43.96	26.22	2.35
	16	47.64	25.14	2.11
	17	40.64	24.85	2.15
	18	41.92	21.32	2.18
	19	39.28	20.94	2.02
	20	36.32	19.4	1.86
	21	44.53	18.7	2.05
	22	55.89	18.56	1.92
	23	54.72	17.59	1.99
	24	39.88	16.62	2.01
	25	46.93	16.15	2.03
	26	39.89	15.44	1.78
	27	47.3	13.96	1.83
	28	59.96	13.15	1.86
	29	54.12	12.31	2.07
	30	60.23	12.10	1.78
	31	40.38	9.27	1.97





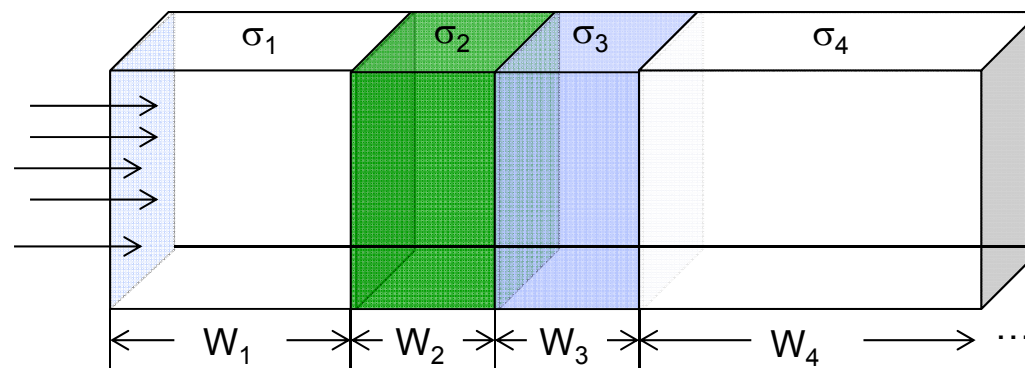
DNA damage studies

- ❑ Cross sections can be calculated for the bases, sugars and phosphates.
- ❑ In this case, the medium is considered a succession of homogeneous media.

$$dI = -IN\sigma dx$$

$$\ln(I / I_0) = -\int_0^x \sigma(u) N du$$

$$I = I_0 \exp \left\{ -N \left[\sum_{j=1}^{i-1} (\sigma_j - \sigma_i) W_j + \sigma_i x \right] \right\}$$

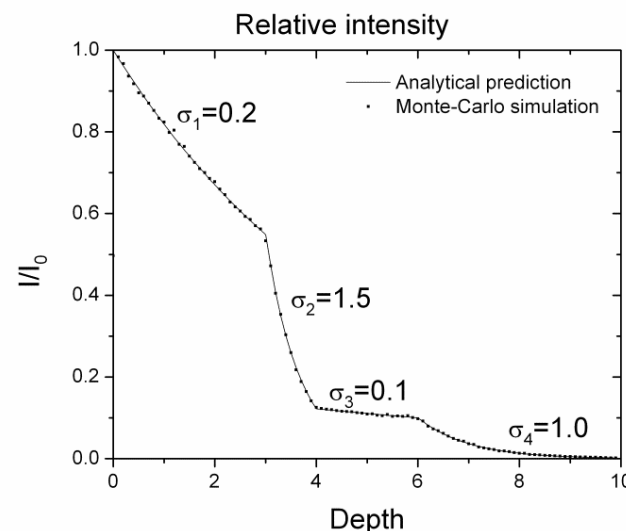


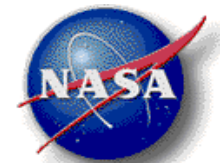
Relative weight

$$p_i = I_0 \frac{\exp(-N \sum_{j=1}^{i-1} W_j \sigma_j) (1 - \exp(-N W_i \sigma_i))}{N \sigma_i}$$

Sampling of W_s

$$W_s = \sum_{j=1}^{i-1} W_j - \frac{1}{N \sigma_i} \log[1 - V(1 - e^{-\sigma_j N W_j})]$$





Radiation chemistry

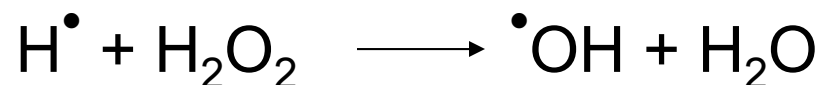
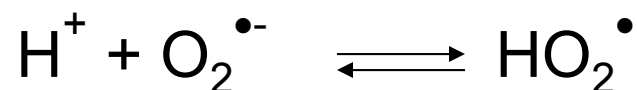
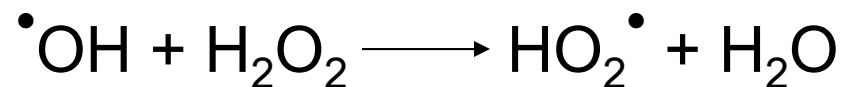
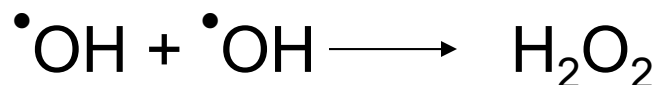
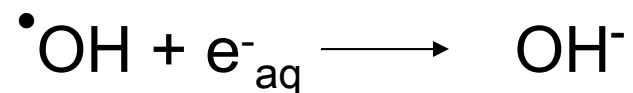
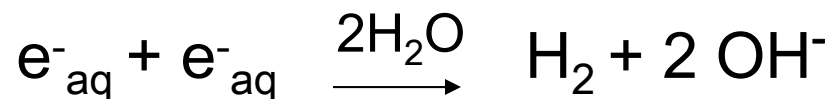
□ $\sim 10^{-12} - 10^{-6} \text{ s}$

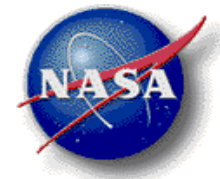
- Particles diffusion
- Chemical reactions

$$G(X) = \frac{\text{Number of chemical species created}}{100 \text{ eV deposited energy}}$$

□ The radiolytic species are not uniformly distributed.
Therefore, an approach based on Green's functions of the diffusion equation (DE) is used.

Examples of chemical reactions:





Bimolecular reactions

□ DE for the propagation of particles A and B

$$\begin{aligned} & \partial p(\mathbf{r}_A, \mathbf{r}_B, t | \mathbf{r}_{A0}, \mathbf{r}_{B0}, t_0) / \partial t \\ &= \left[D_A \nabla_A^2 + D_B \nabla_B^2 \right] p(\mathbf{r}_A, \mathbf{r}_B, t | \mathbf{r}_{A0}, \mathbf{r}_{B0}, t_0) \end{aligned}$$

$p(\mathbf{r}_A, \mathbf{r}_B, t | \mathbf{r}_{A0}, \mathbf{r}_{B0}, t_0)$: probability of particles A and B to be at positions $\mathbf{r}_A$ and $\mathbf{r}_B$ at time t , given that they were at $\mathbf{r}_{A0}$ and $\mathbf{r}_{B0}$ at t_0

D_A, D_B : Diffusion coefficients

□ Transformation

$$\mathbf{R} = \sqrt{D_B / D_A} \mathbf{r}_A + \sqrt{D_A / D_B} \mathbf{r}_B \quad \nabla_{\mathbf{R}} = \partial / \partial \mathbf{R}$$

$$\mathbf{r} = \mathbf{r}_B - \mathbf{r}_A \quad \nabla_{\mathbf{r}} = \partial / \partial \mathbf{r}$$

$$\partial p(\mathbf{R}, \mathbf{r}, t | \mathbf{R}_0, \mathbf{r}_0, t_0) / \partial t = (D_A + D_B) \left[\nabla_{\mathbf{R}}^2 + \nabla_{\mathbf{r}}^2 \right] p(\mathbf{R}, \mathbf{r}, t | \mathbf{R}_0, \mathbf{r}_0, t_0)$$

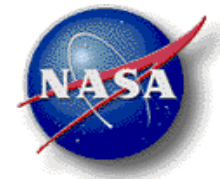
$$p(\mathbf{R}, \mathbf{r}, t | \mathbf{R}_0, \mathbf{r}_0, t_0) = p^{\mathbf{R}}(\mathbf{R}, t | \mathbf{R}_0, t_0) p^{\mathbf{r}}(\mathbf{r}, t | \mathbf{r}_0, t_0)$$

$$\partial p^{\mathbf{R}}(\mathbf{R}, t | \mathbf{R}_0, t_0) / \partial t = (D_A + D_B) \nabla_{\mathbf{R}}^2 p^{\mathbf{R}}(\mathbf{R}, t | \mathbf{R}_0, t_0)$$

$$\partial p^{\mathbf{r}}(\mathbf{r}, t | \mathbf{r}_0, t_0) / \partial t = (D_A + D_B) \nabla_{\mathbf{r}}^2 p^{\mathbf{r}}(\mathbf{r}, t | \mathbf{r}_0, t_0)$$

Uncoupled equations

in $\mathbf{r}$ and $\mathbf{R}$



Bimolecular reactions

□ Free diffusive motion of the coordinate $\mathbf{R}$

$$\partial p^{\mathbf{R}}(\mathbf{R}, t | \mathbf{R}_0, t_0) / \partial t = D \nabla_{\mathbf{R}}^2 p^{\mathbf{R}}(\mathbf{R}, t | \mathbf{R}_0, t_0) \quad (\text{DE})$$

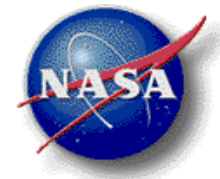
$$p^{\mathbf{R}}(\mathbf{R}, t | \mathbf{R}_0, t_0) = \delta(\mathbf{R} - \mathbf{R}_0) \quad (\text{Initial condition})$$

$$p^{\mathbf{R}}(|\mathbf{R}| \rightarrow \infty, t | \mathbf{R}_0, t_0) = 0 \quad (\text{Boundary condition})$$

$$p^{\mathbf{R}}(\mathbf{R}, t | \mathbf{R}_0, t_0) = \frac{1}{[4\pi D(t - t_0)]^{3/2}} \exp\left[-\frac{(\mathbf{R} - \mathbf{R}_0)^2}{4D(t - t_0)}\right] \quad (\text{Solution})$$

$p^{\mathbf{R}}(\mathbf{R}, t | \mathbf{R}_0, t_0)$: probability distribution of the vector $\mathbf{R}$ at time t , given that it was located at position $\mathbf{R}_0$ at time t_0

$D = D_A + D_B$: Sum of the diffusion coefficients



Bimolecular reactions

□ Free diffusive motion* of the inter-particle separation vector $\mathbf{r}$

$$\frac{\partial p^{\mathbf{r}}(\mathbf{r}, t | \mathbf{r}_0, t_0)}{\partial t} = D \nabla_{\mathbf{r}}^2 p^{\mathbf{r}}(\mathbf{r}, t | \mathbf{r}_0, t_0) \quad (\text{DE})$$

$$p^{\mathbf{r}}(\mathbf{r}, t | \mathbf{r}_0, t_0) = \delta(\mathbf{r} - \mathbf{r}_0) \quad (\text{Initial condition})$$

□ For chemical reactions, we need the inter-particle distance r .

- Therefore, the DE is written in spherical coordinates.
- Only the radial component will be considered (angular dependency terms are neglected). This considerably simplifies the analytical solution.

$$\frac{\partial p(r, t | r_0)}{\partial t} = \frac{D}{r^2} \frac{\partial}{\partial r} \left[r^2 \frac{\partial}{\partial r} p(r, t | r_0) \right] \quad (\text{Radial part of the DE})$$

$$4\pi r_0^2 p(r, t | r_0) = \delta(r - r_0), r \geq R \quad (\text{Initial condition; } R = \text{reaction radius})$$

$p(r, t | r_0, t_0)$: probability distribution of the separation distance r at time t , given that it was r_0 at time t_0



Bimolecular reactions

□ Simple case: reaction with rate k_a



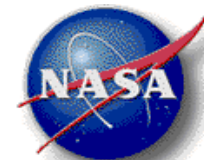
$$4\pi R^2 D \left. \frac{\partial p(r, t | r_0)}{\partial r} \right|_{r=R} = k_a p(R, t | r_0) \quad (\text{Boundary condition})$$

$$4\pi r r_0 p(r, t | r_0) = \frac{1}{\sqrt{4\pi Dt}} \left\{ \exp\left[-\frac{(r-r_0)^2}{4Dt}\right] + \exp\left[-\frac{(r+r_0-2R)^2}{4Dt}\right] \right\} + \alpha W\left(\frac{r+r_0-2R}{\sqrt{4Dt}}, -\alpha\sqrt{Dt}\right) \quad (\text{Green's function})$$

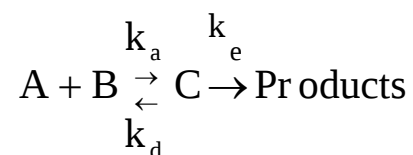
$$Q(t | r_0) = \int_R^\infty 4\pi r^2 p(r, t | r_0) dr = 1 + \frac{R\alpha + 1}{r_0\alpha} \left[W\left(\frac{r_0 - R}{\sqrt{4Dt}}, \alpha\sqrt{Dt}\right) - \text{Erfc}\left(\frac{r_0 - R}{\sqrt{4Dt}}\right) \right] \quad (\text{Survival probability})$$

$$\alpha = -\frac{k_a + 4\pi RD}{4\pi R^2 D}$$

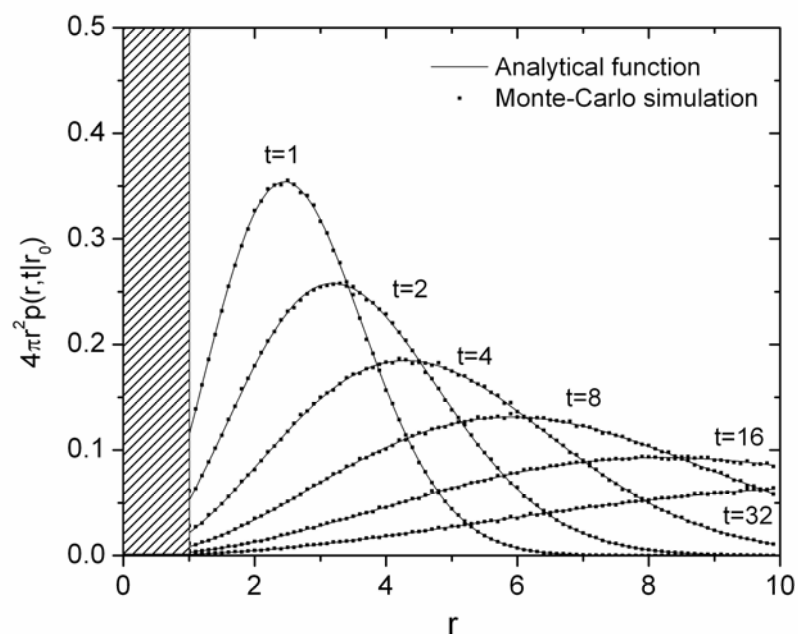
The probability of reaction $P(t|r_0) = 1 - Q(t|r_0)$. At each time step, the probability of reaction is assessed. If the particles have not reacted, their relative distance is obtained by sampling the Green's function.



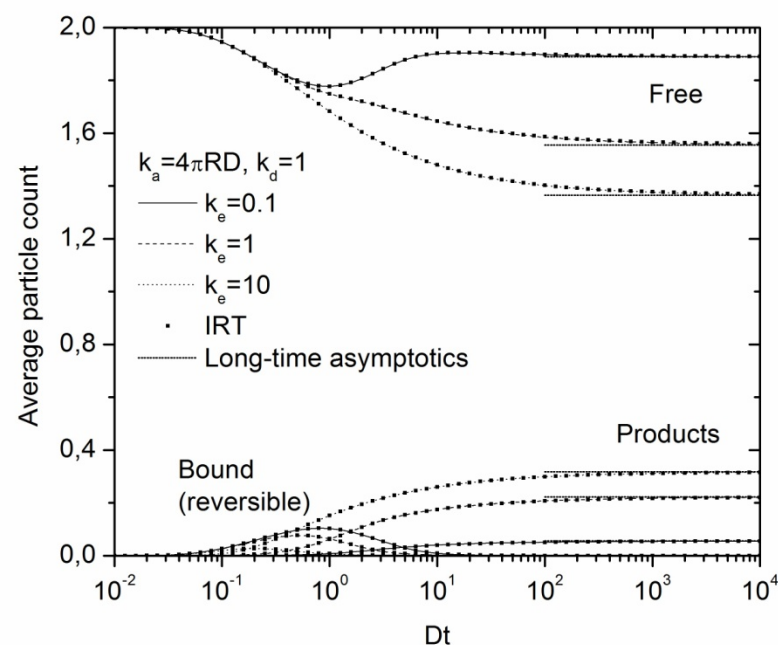
Green's function for radiation chemistry

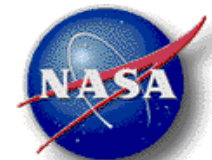


Green's functions

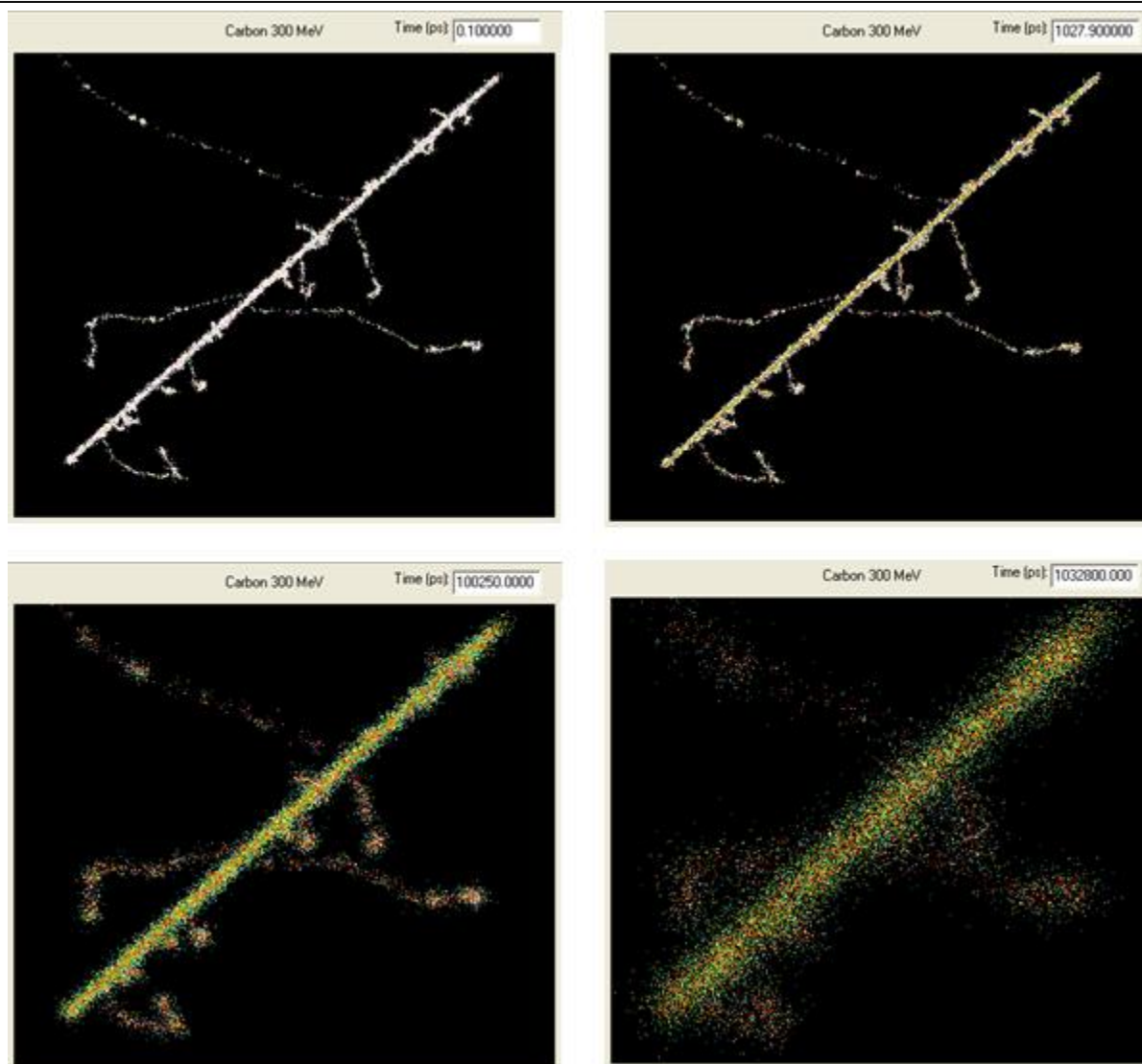


Survival and binding probabilities





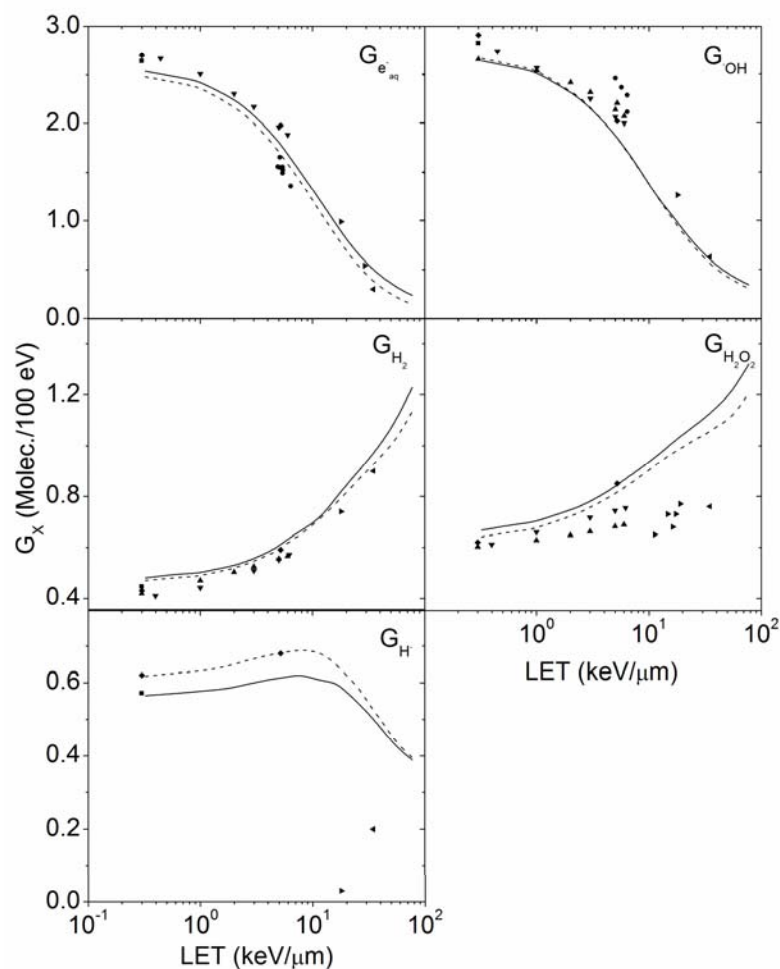
Radiation chemistry





Radiation chemistry

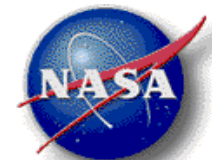
Primary yields of e_{aq}^- , $\cdot OH$, $H\cdot$, H_2 and H_2O_2 as a function of the LET



Irradiation by 300-0.1 MeV protons

LET: ~ 0.3 -85 keV/μm

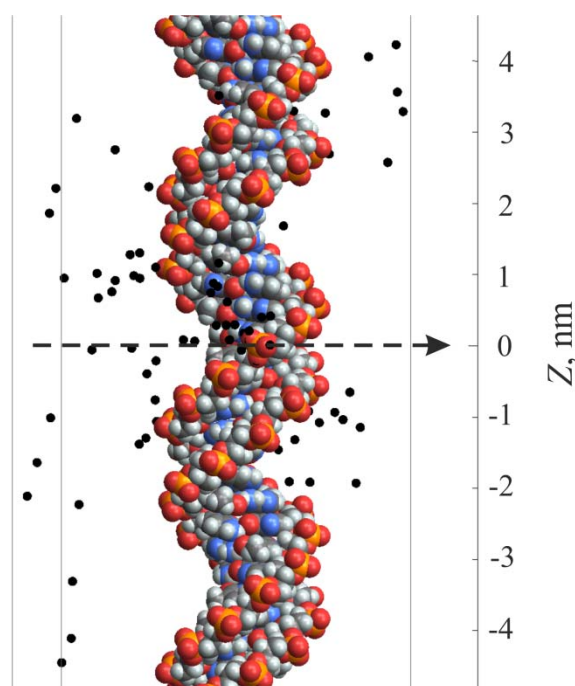
Note: the primary yields (noted G_x) are the yields at the end of spur expansion ($\sim 10^{-6}$ s)



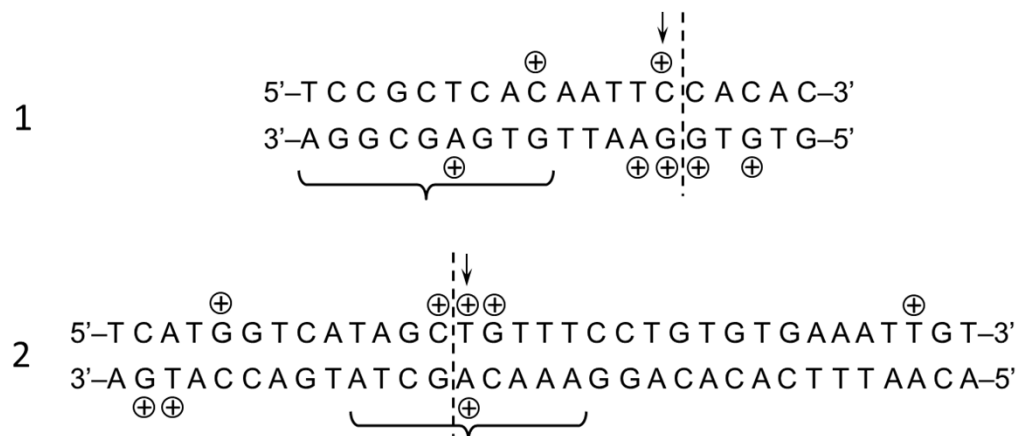
Charge migration in DNA

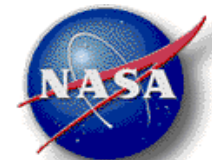
□ Determination of charge creation sites

Intersection of DNA strand and track structure (1 GeV/u iron ion)



DNA sequences and initial charges locations

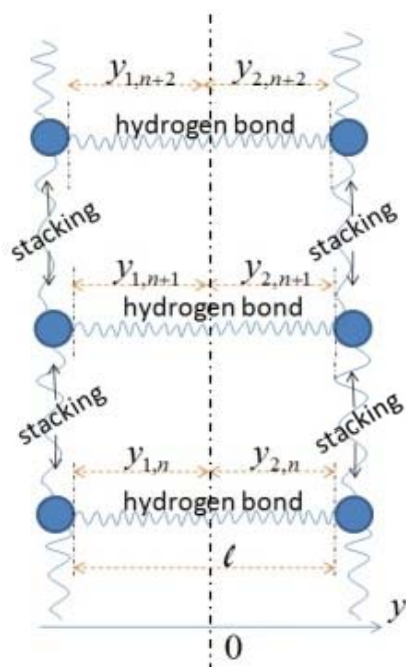




Charge migration in DNA

□ Semi-classical quantum mechanical DNA model of charge migration

Double stranded model of DNA



Hamiltonian

$$H = H_{Cl} + \langle \psi | H_Q | \psi \rangle,$$

$$H_{Cl} = \sum_{n=1}^N \left(\frac{M \dot{y}_{1,n}^2}{2} + \frac{M \dot{y}_{2,n}^2}{2} + \frac{k_v (y_{1,n} - y_{1,n-1})^2}{2} + \frac{k_v (y_{2,n} - y_{2,n-1})^2}{2} + \frac{k_v (y_{1,n} - y_{2,n} + l)^2}{2} \right)$$

$$H_Q = \sum_{n=1}^N \left(\alpha_n^0 + \alpha_n' (y_{1,n} - y_{2,n} + l) \right) |n\rangle \langle n| + \sum_{n \neq m}^N v_{n,m} |n\rangle \langle m|$$

$$\varepsilon_n = \alpha_n^0 + \alpha_n' (v_{+} - v_{-} + l),$$

Schrodinger equation

$$i\hbar \frac{\partial |\psi\rangle}{\partial t} = H_Q |\psi\rangle$$

$$|\psi\rangle = \sum_{n=1}^N b_n(t) |n\rangle.$$

Hamilton equations

$$M \frac{\partial^2 y_{1,n}}{\partial t^2} = - \frac{\partial H}{\partial y_{1,n}} - \gamma \frac{\partial y_{1,n}}{\partial t},$$

$$M \frac{\partial^2 y_{2,n}}{\partial t^2} = - \frac{\partial H}{\partial y_{2,n}} - \gamma \frac{\partial y_{2,n}}{\partial t},$$

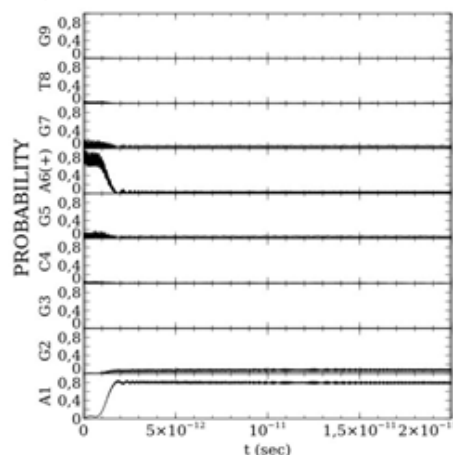


Charge migration in DNA

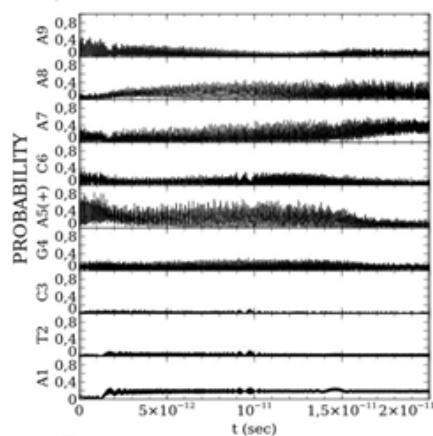
□ Semi-classical quantum mechanical DNA model of charge migration

Time-dependent positive charge location

a) A1 G2 G3 C4 G5 A6(+) G7 T8 G9

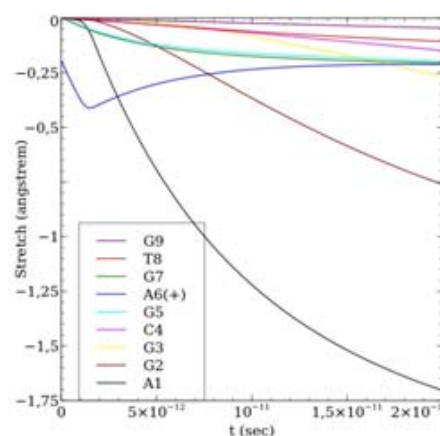


b) A1 T2 C3 G4 A5(+) C6 A7 A8 A9

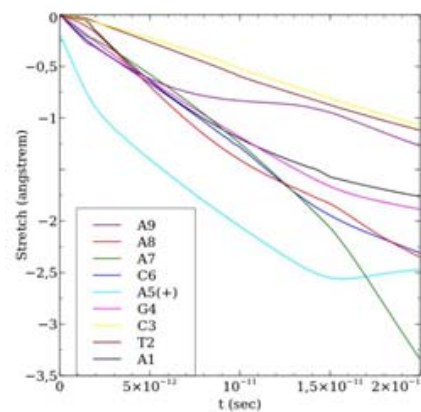


DNA base pairs stretch

a) A1 G2 G3 C4 G5 A6(+) G7 T8 G9



b) A1 T2 C3 G4 A5(+) C6 A7 A8 A9

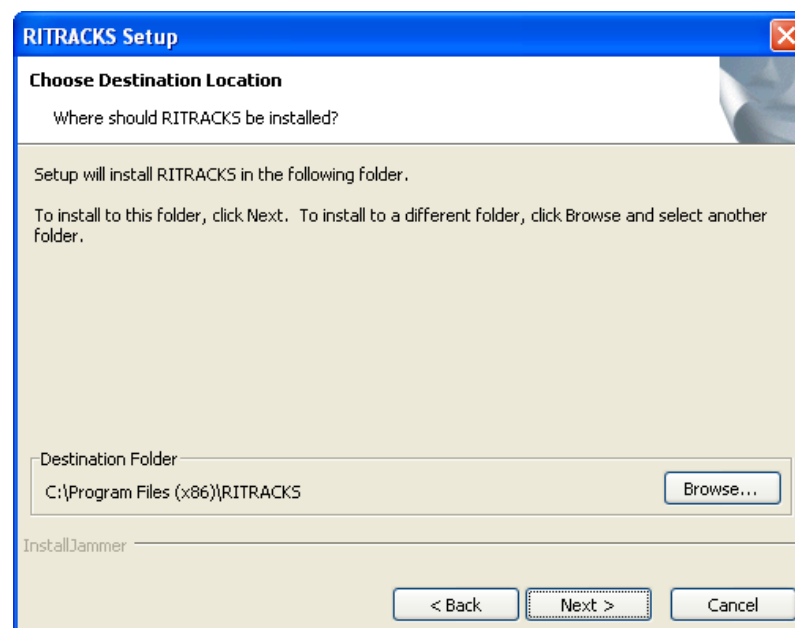
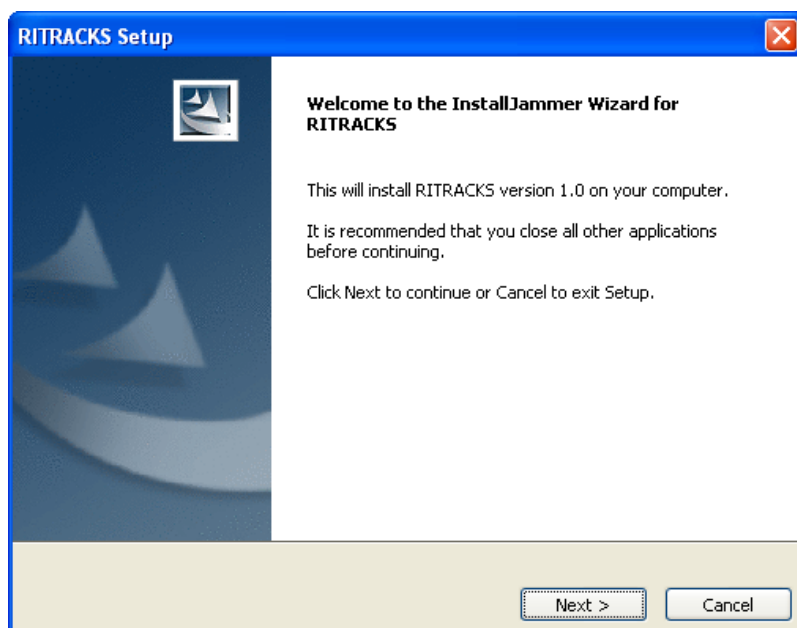


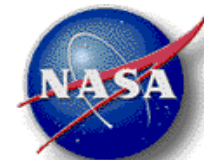


Using RITRACKS

❑ The installer

- The necessary files are included in an installer created by the freeware InstallJammer
- The program is installed in the folder C:\Program Files (x86)\RITRACKS
- Simulations are stored the subfolder RITRACKS Simulations in the My Documents folder





RITRACKS main window

RITRACKS 1.0 [Minimize] [Maximize] [Close]

File Data View Options Help

Incident radiation

☐ Electron

☒ Ion 12C6+ ▼

Energy: 25 MeV/amu

LET (appr): 78.27 keV/um

More

Irradiation volume

☒ Disk ☐ Clip tracks

☐ Square

No particles: 1

Radius: 0 um

Length: 5 um

Area: - cm²

Fluence: - cm⁻²

Dose (appr): - cGy

Messages

Welcome to RITRACKS

Simulation info

Histories: 10

Calculations

☒ Save track structure

☐ Save all events

☒ Save 3D dose map

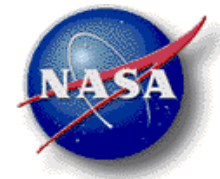
Start simulation

3D tracks

Simulation progress:

Before simulation

Results details



Radiation info window

The following information is given in this window

Rest mass energy: Mc^2

Total energy: γMc^2

Relativistic γ : $\gamma = T / Mc^2 + 1$

Relativistic β : $\beta^2 = 1 - 1/\gamma^2$

Momentum: $p = \gamma Mv$

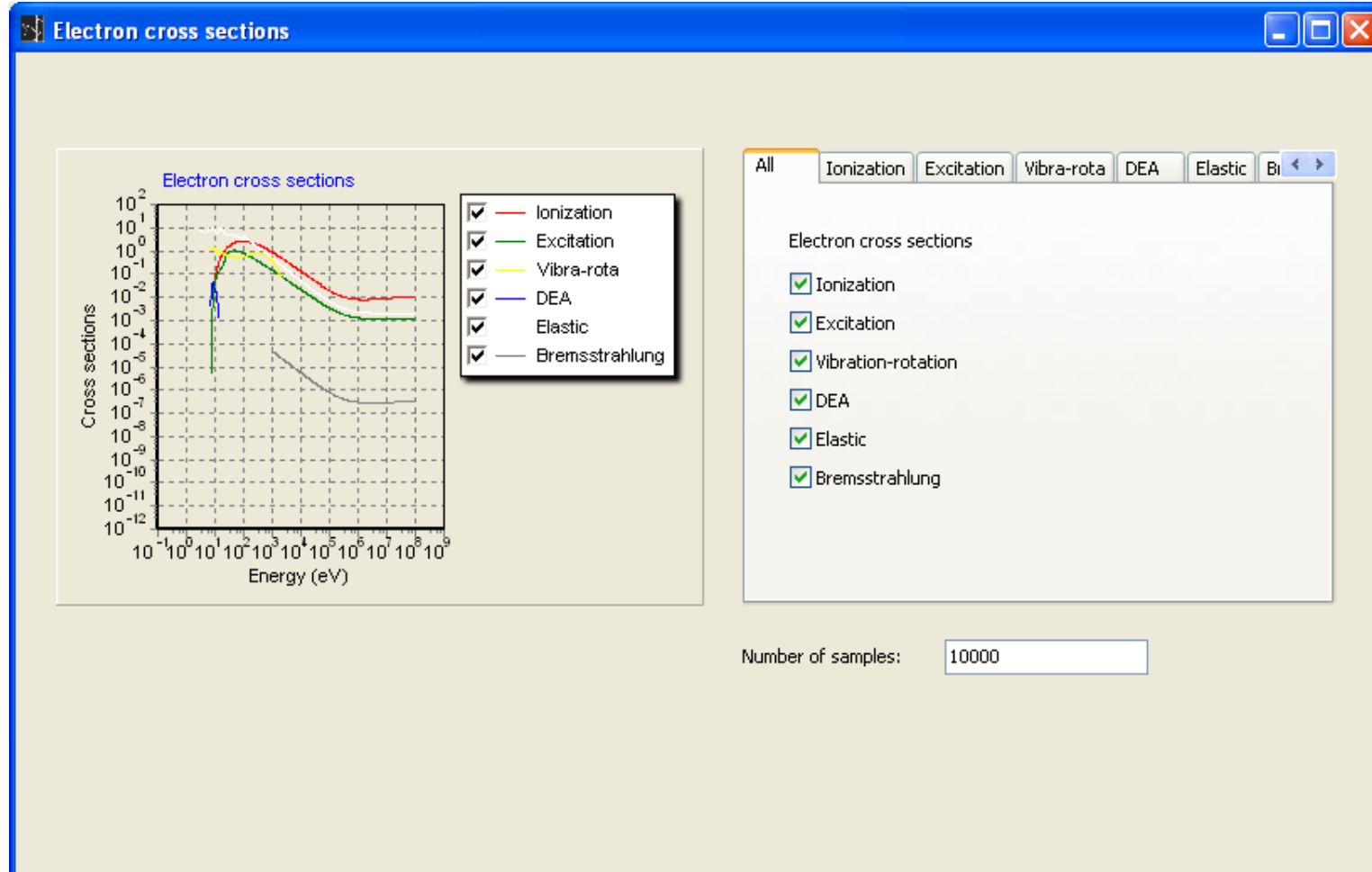
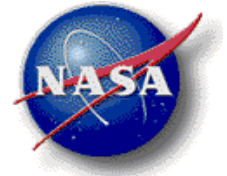
Maximum energy
Transfer to e^- : $E_{\max} = \frac{2mc^2(\gamma^2 - 1)}{1 + 2\gamma(m/M) + (m/M)^2}$

LET (MeV/cm):
(Bethe) $-\frac{dE}{dx} = \frac{0.170}{\beta^2} [F(\beta) - 4.31]$

Radiation info		
Radiation type:	Ion	$^{12}_C^{6+}$
Kinetic energy	25	MeV/amu
Rest mass energy	11258.939814	MeV
Total energy	11558.940988	MeV
β^2	0.051234	
β	0.22635	
γ	1.026646	
p	2616.36982	MeV/c
Qmax	55.127	keV
Zeff	6	
LET (appr)	78.27	keV/um

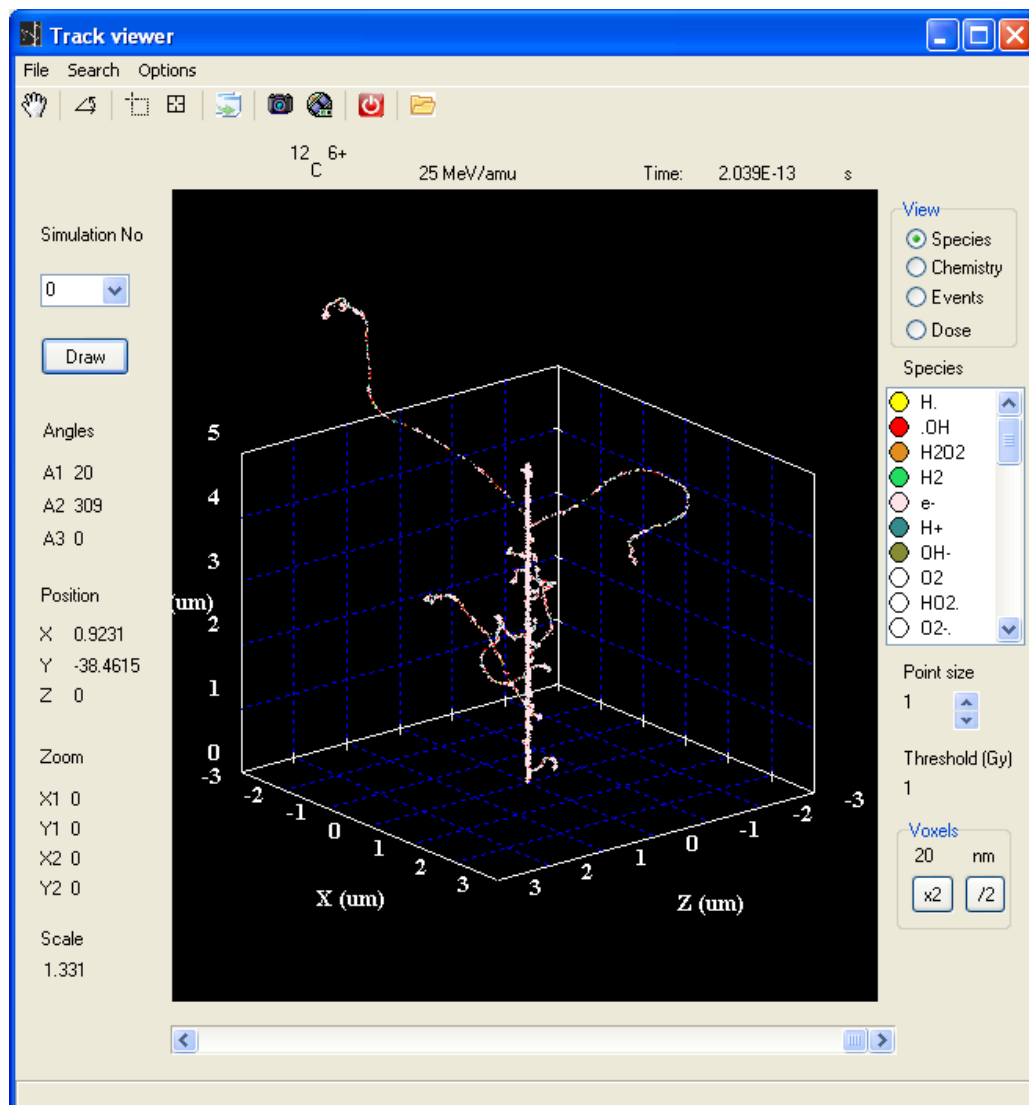
$$F(\beta) = \ln \frac{1.02 \times 10^6 \beta^2}{1 - \beta^2} - \beta^2$$

Electron cross sections window





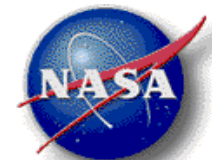
Visualization window



- Tools:
- Rotation
 - Translation
 - Zoom
 - Save to file
 - Copy to clipboard
 - Create a .avi file
 - Open data folder

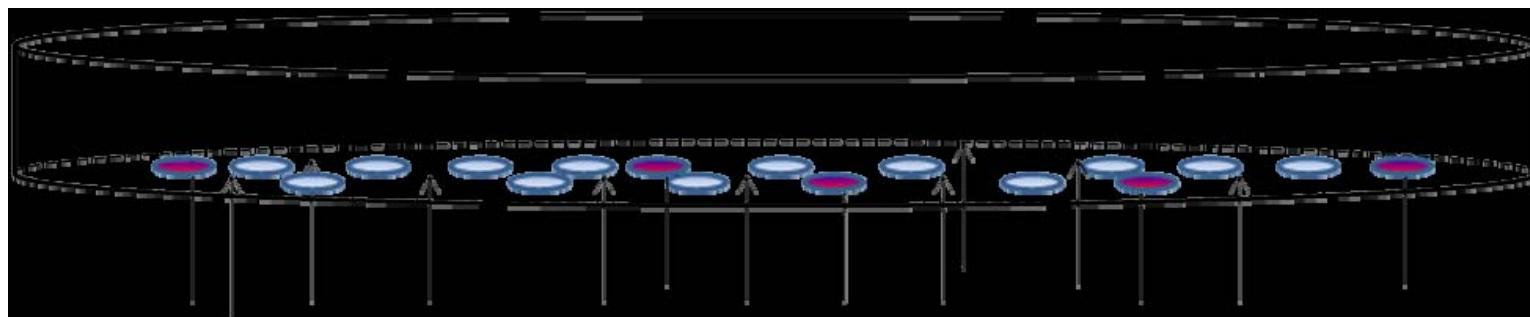
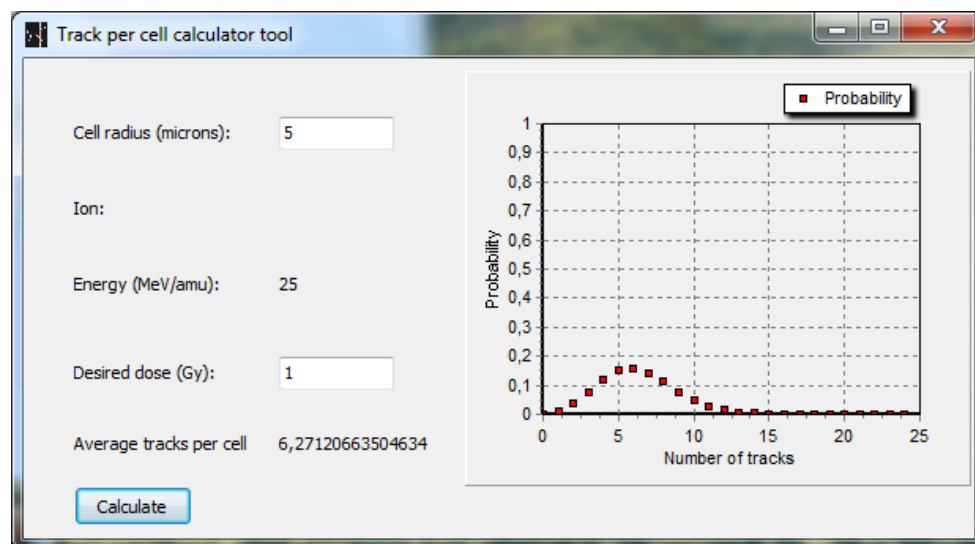
- Visualization:
- Radiolytic species
 - Events
 - Dose (voxels)

Time evolution



RITRACKS tools

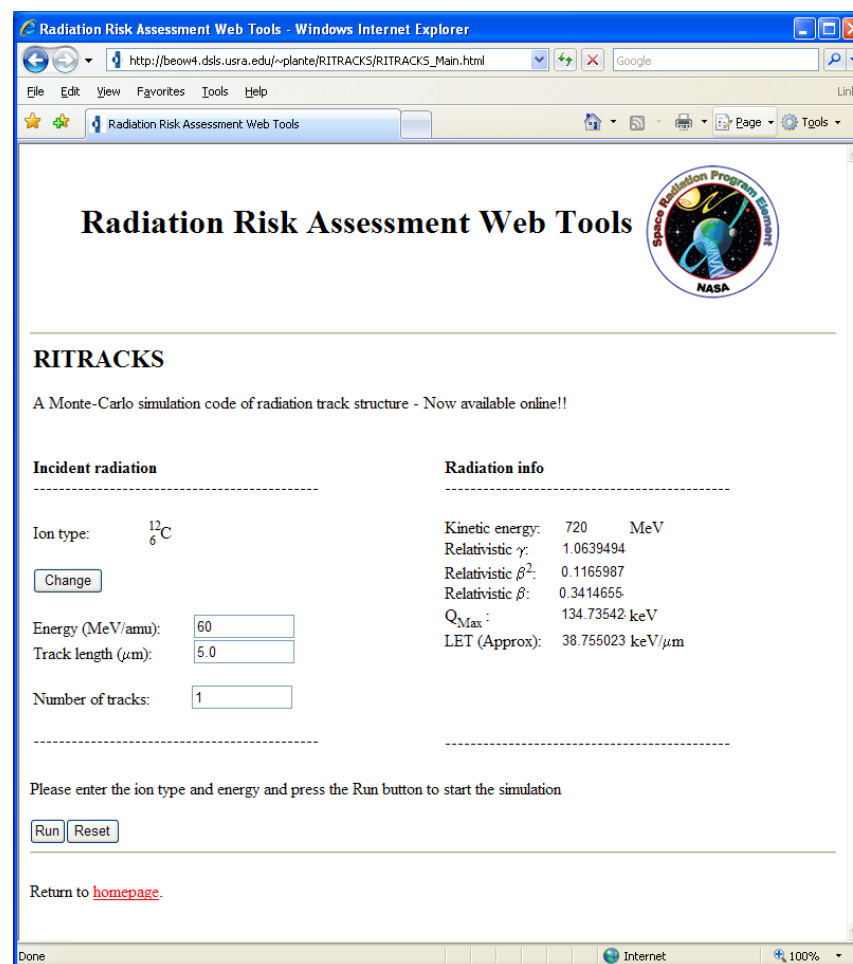
- ❑ Calculation of tracks per cell in a cell culture for a given ion, energy and dose



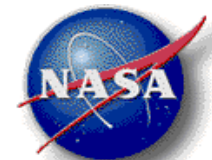


Release history

- ❑ RITRACKS was used by the students at the NASA Space Radiation Summer School at the Brookhaven National Laboratory, Upton, New York (June 6-24, 2011, May 28 - June 15, 2012, MIT ICED June 2012)(over 40 users)
- ❑ The release to international partners was approved in 2011
- ❑ RITRACKS was released to NASA space radiation community with over 20 users
- ❑ The software is now available for download on the web site <http://spaceradiation.usra.edu/irModels/> (ITAR, authentication and password required)

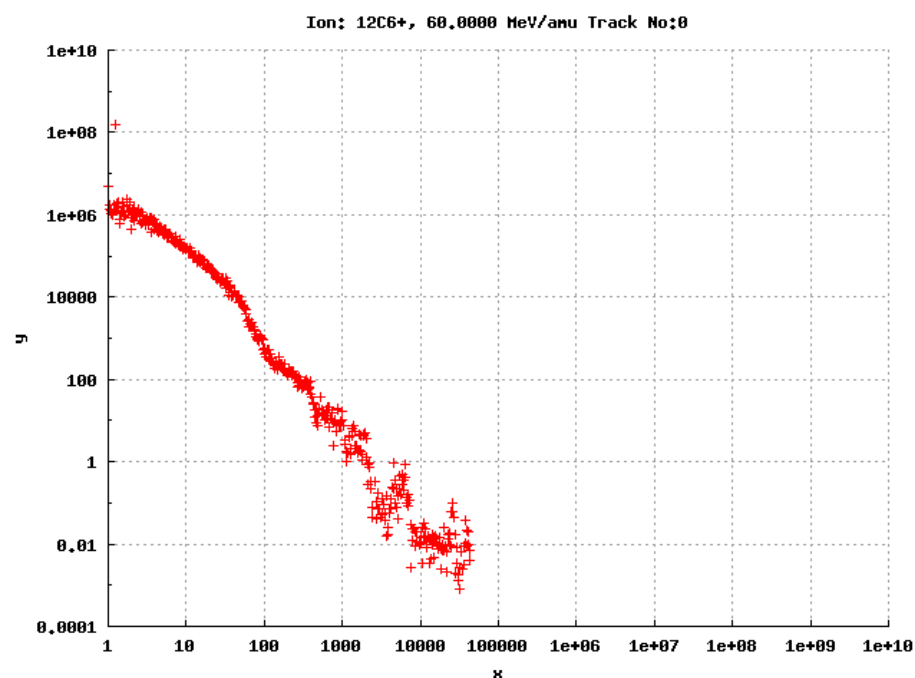
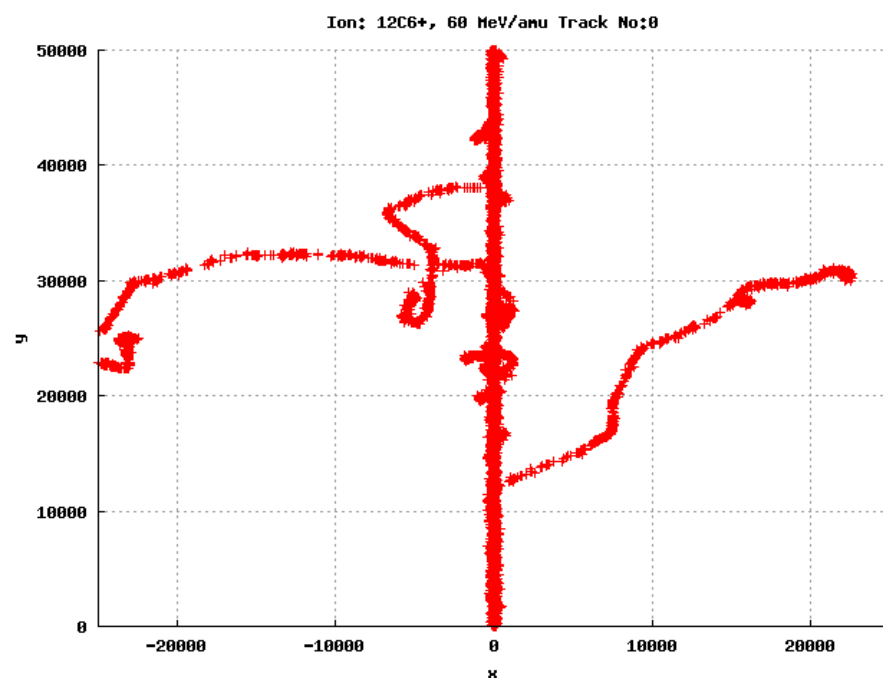


<http://spaceradiation.usra.edu>



Release history

❑ An online version of RITRACKS will be available soon!

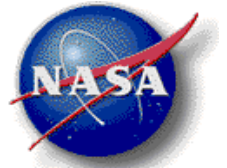


Left: Simulation of a $^{12}\text{C}^{6+}$, 60 MeV/amu, on the projected RRAW site.

Right: Calculation of the radial dose for the track depicted on the left

The track structure data and the radial dose are available for download after calculation

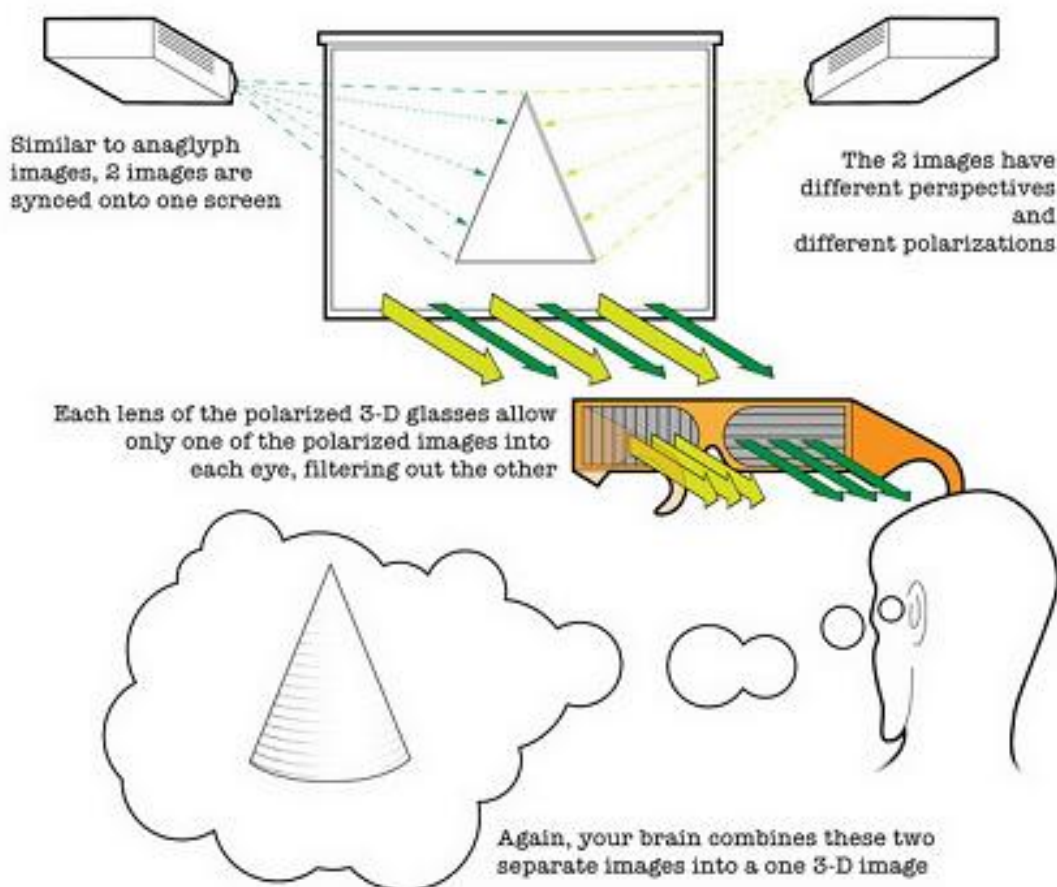
While waiting for holograms...



Future plans for development and use

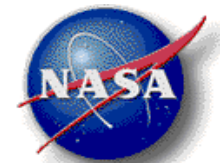
❑ 3D stereoscopic computer models

Polarized 3-D Glasses



The track appears as a floating object in front of the computer!

It could be interesting to use this approach for proteins, DNA and other cellular structures



Future plans for development and use

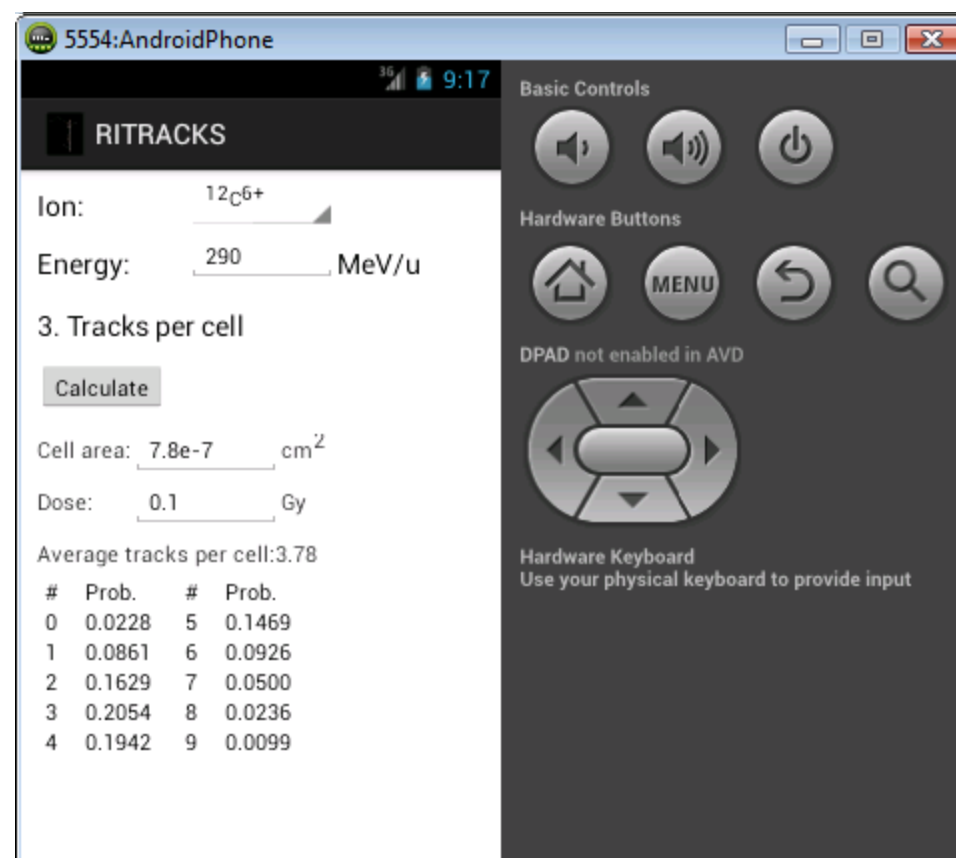
☐ Android/iPhone version

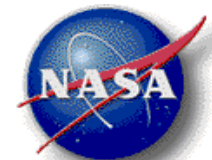
☐ For ions:

- LET
- Relativistic β and γ
- Z_{eff} and Z_{eff}^2/β^2
- Maximum energy transfer to an electron
- Dose and fluence
- Radial dose
- Number of hits per cell
- in a cell culture

☐ For electrons:

- Relativistic β and γ
- Range





Future plans for development and use

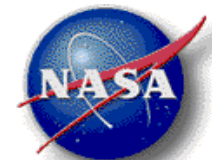
- ☐ **Implementation of the non-homogeneous chemistry**
- ☐ **Predictions of clustered and complex DNA damage yields in human cells for improving the understanding of DNA repair and signal transduction**
- ☐ **Use with chromosome models to study double-strand breaks (DSB) in relation to cancer risks from space radiation**
- ☐ **Web-based version**
- ☐ **New GPU-CPU version to improve computational speeds by several orders of magnitude.**



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- ☐ USRA
- ☐ NASA





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